Eastern Allergy Conference
May 29 - June 1, 2025 ~ Palm Beach, FL

Scientific Posters F1-F46 will be on display in the Ponce Foyer during the coffee break, 10:00-10:45am, Friday May 30, 2025

Not for CME Credit

F1

Lymphoma patients with IgE deficiency have lower rates of remission compared with non-IgE deficient individuals: a pilot retrospective study

Kaitlyn, Morio, MD; Simon, Zhen, MD; Denisa, Ferastraoaru, MD

Introduction: Studies show that patients with IgE deficiency (IED, IgE<2.5 kU/L) have higher rates and risk of cancer. It is not known if IgE levels are important in cancer outcomes. This retrospective pilot study compared remission rates between IED and non-IED lymphoma patients.

Methods: Chart review was performed on 55 lymphoma patients who had IgE measured prior to cancer diagnosis at Montefiore Medical Center, Bronx, NY between 2008-2022. Data about the type of lymphoma, treatment and remission was collected and analyzed.

Results: Out of 55 lymphoma patients, 6 had IED prior to lymphoma diagnosis. The mean IgE level in non-IED individuals was 656±1398 kU/L. The time between IgE measurement and lymphoma diagnosis was 27.5±22.4 months in IED patients and 35.2±34.8 months in non-IED individuals. Lymphoma types in IED patients were non-Hodgkin B-cell lymphoma (5/6, 83%) and adult T-cell lymphoma (1/6,13.3%). Non-Hodgkin B-cell lymphoma was also the most common in non-IED individuals (34/49, 69.4%), followed by non-Hodgkin T-cell lymphoma (6/49, 12.2%) and Hodgkin lymphoma (5/49, 10.2%). Those patients who were found IED prior to lymphoma diagnosis were less likely to reach remission when compared to non-IED patients (OR=0.04, 95%CI: 0.004-0.472, p=0.01). Both groups had normal levels of other immunoglobulin isotypes. We found similarly low rates of common variable immunodeficiency in IED (0%) and non-IED (3/49, 6.1%, p=0.5) patients.

Conclusions: This pilot study suggests that IgE levels might be important in lymphoma outcomes, with IED patients having significantly lower remission rates. Larger prospective studies are needed to further explore this finding.

F2

A Retrospective Case Series of Novel Unusual Phenotypes of Food Protein-Induced Enterocolitis

Danielle Harrison, MD, Kirsi M. Järvinen, MD, PhD

Introduction: Food protein-induced enterocolitis syndrome (FPIES) is a delayed, non-IgE-mediated food allergy (FA), which in its atypical presentation switches to an IgE-mediated FA over time.

Objective: To describe children with various unusual phenotypes of FPIES: FPIES switching to IgE-mediated FA/food sensitization, IgE-mediated FA/sensitization switching to FPIES, and FPIES with concurrent IgE sensitization.

Methods: We conducted a retrospective chart review of all <12 mo pediatric cases seen since 2014 for suspicion of FA diagnosed with FPIES at our academic pediatric allergy clinic. A total number of 90 cases were reviewed. The charts were reviewed for the initial presentation of FPIES and other atopic comorbidities, including IgE-mediated FA and sensitization. The pediatric cases were followed until their most recent clinic visit to evaluate the outgrowth of FPIES/FA or evolution to other atopic phenotypes.

Results: Five cases had an initial presentation of FPIES, who later developed IgE-mediated FA (n=2), most commonly for egg, or food sensitization with unknown clinical relevance (n=3) to the same trigger food as previously described. There were five cases with initial presentation of IgE-mediated FA (n=3)/food sensitization (n=2), who later developed FPIES to the same trigger (most commonly egg and milk). Finally, nine cases had an initial presentation of FPIES with concurrent IgE sensitization to the same trigger food, three of which later developed IgE-mediated FA to the same culprit food trigger (most commonly peanut and egg).

Conclusion: This case series describes novel unusual FPIES cases, including the progression from IgE-mediated FA to FPIES, which adds to the limited literature on the overlap between IgE- and non-IgE-mediated FA.

F3

When Water Becomes Harmful: A Prickling Mystery of Aquagenic Pruritus and its Psychosocial Burden

Dilpreet Singh, MD

Aquagenic pruritus (AP) is a rare, non-lesional dermatosis characterized by intense, water-induced itching in the absence of visible skin changes. Symptoms typically develop within 15 minutes of exposure—regardless of water temperature—and resolve spontaneously within one to two hours. While most commonly associated with polycythemia vera and other myeloproliferative neoplasms, AP has been infrequently linked to immunologic and systemic disorders.

We report a case of a 26-year-old African American male with hereditary elliptocytosis who presented with a two-year history of water-triggered pruritus. Symptoms were described as “pins and needles” and affected the torso, back, upper arms, and thighs following exposure to sweat, showers, rain, and chlorinated pools. No rash, urticaria, or mucosal involvement was noted. The patient denied exposure to new detergents, medications, or allergens.

Comprehensive evaluation—including CBC, metabolic panel, liver function, ANA, complements, tryptase, histamine, IgE, and skin prick testing—was unrevealing. JAK2 mutation undetected. First-line treatments, including non-sedating antihistamines and emollients, were ineffective. Neuromodulatory therapies also failed to provide relief. Due to significant psychosocial burden, he developed depression requiring SSRIs and cognitive behavioral intervention.

While complete avoidance of water was impractical, symptom mitigation strategies—such as minimizing exposure to temperature extremes and high-pressure water streams—was utilized. Notably, the patient reported partial symptom control with a combination of above, levocetirizine and omalizumab, suggesting a possible IgE-independent mast cell component. Emerging evidence suggests that beta-blockers, B-alanine, calamine, SSRIs, and psychological support may provide adjunctive benefits.

This case highlights the diagnostic and therapeutic challenges of AP. Though rare, AP should prompt evaluation for underlying hematologic or immunologic disorders, and the lack of definitive treatment can be physically and mentally distressing. Multidisciplinary management is essential to address both dermatologic and psychiatric sequelae.

F4

Quantifying Ocular Allergic Redness in a Controlled Allergen Challenge Environment Using a Smartphone-Based Imaging Platform

Mark B. Abelson M.D, Ethan Bensinger Ph.D., Paul Gomes Ph.D.

Introduction: Allergic conjunctivitis is a common condition characterized by ocular redness and itching triggered by seasonal allergens such as ragweed and timothy grass. Field-based studies are often limited by variable allergen exposure. Controlled allergen exposure environments offer a standardized approach for inducing allergic responses and evaluating clinical endpoints. This study assessed the ability of a mobile allergen exposure chamber to provoke ocular allergic symptoms and utilized a smartphone-based imaging platform to quantify changes in conjunctival redness.

Methods: Seventeen subjects with a self-reported history of seasonal allergic conjunctivitis (SAC) for at least two consecutive years and a positive skin test to ragweed or timothy grass within the past 24 months were screened. At the second study visit, participants were exposed for 90 minutes to either ragweed or timothy grass pollen inside a mobile allergen chamber (Ora Mobile Allergy Biocube®). Standardized photographs of the inferior conjunctiva were captured before and after exposure using a smartphone-based imaging system (Ora EyeCup™). Images were segmented and scored for ocular redness. Low-quality images or those with segmentation errors were excluded, yielding 18 eyes from 11 subjects for analysis.

Results: The mean increase in conjunctival redness following exposure was 6.58 units (SD = 5.27). A Wilcoxon signed-rank test comparing pre- and post-exposure redness scores showed a statistically significant increase ($p = 0.00038$), confirming successful induction of an ocular allergic response.

Conclusions: A mobile controlled allergen exposure environment successfully elicited quantifiable allergic conjunctival responses. The smartphone-based imaging platform provided objective, reproducible measurements of ocular redness, supporting its potential for use in clinical studies evaluating allergy-related endpoints.

F5

First Reported Real World Clinical Anaphylaxis Treated with Neffy: A Case Series

Jake Rosenblum DO, Gregory Puglisi MD, Joseph Grillo MD

Introduction: Oral graded food challenges (OGFC) are the gold standard in evaluation of IgE-mediated food allergies and are frequently performed in the outpatient clinical setting. Subcutaneous Immunotherapy (SCIT) is a widely used treatment for allergic rhinitis and asthma. Both SCIT and OGFC can result in anaphylactic reactions requiring rapid intervention. Epinephrine, the first-line treatment for anaphylaxis, is typically administered via intramuscular (IM) injection. Neffy nasal spray, a novel epinephrine delivery system, was FDA approved in August 2024 as a non-injection alternative for managing anaphylaxis in adult and pediatric patients. There is limited published usage of Neffy outside of clinical trials, this case series offers firsthand experience of Neffy treatment in the field.

Methods: This case series is a compilation of five patients (1 male and 4 female) in our clinic aged 22-57 who experienced systemic reactions. Each patient was treated with Neffy for symptoms after doses of either SCIT or OGFC in the clinical setting.

Results: Five patients experienced systemic reactions, 3 after SCIT and 2 during OGFC (one peanut and one walnut). Symptoms included flushing, pruritis, abdominal pain, throat tightness, and nasal congestion. All patients were treated with Neffy and experienced prompt symptom resolution. One patient had return of itch and nasal congestion symptoms 20 minutes after Neffy administration prompting a 2nd dose of Neffy in the same nostril resulting in resolution of symptoms. The only observed adverse reaction was a transient feeling of "jitters" in one patient.

Conclusions: We present a unique series of multiple patients who developed anaphylaxis in our clinic after administration of SCIT or during OGFC. All patients had improvement in symptoms with Neffy, highlighting its viability as an alternative to IM injection in managing anaphylactic reactions. To our knowledge, these are the first reported cases of anaphylaxis successfully managed with Neffy outside of a clinical trial.

F6

Long-Term Safety and Efficacy of Oral Deucrictibant for Treatment of Hereditary Angioedema Attacks: Results of the RAPIDe-2 Extension Study

John Anderson M.D., Joshua S. Jacobs M.D., Michael E. Manning M.D., Peng Lu M.D., Ph.D., H. Henry Li M.D., Ph.D.

Introduction: Hereditary angioedema (HAE) attacks are caused by excess bradykinin activating bradykinin B2 receptors. Deucrictibant is a selective, orally administered bradykinin B2 receptor antagonist under development for prophylactic and on-demand treatment of HAE attacks.

Methods: RAPIDe-2 (NCT05396105) is an ongoing, two-part, Phase 2/3 extension study evaluating the long-term safety and efficacy of deucrictibant immediate-release (IR) capsule for on-demand treatment of repeat HAE attacks. RAPIDe-2 Part A enrolled adult participants who completed RAPIDe-1 (NCT04618211). Participants continued to self-administer the same double-blinded dose of deucrictibant IR capsule (10mg, 20mg, or 30mg) received during RAPIDe-1 to treat qualifying attacks including non-severe upper airway attacks presenting without breathing difficulties.

Results: A Part A data snapshot (cutoff: 01 March 2024) included 265 attacks treated with deucrictibant IR capsule by 17 participants. Due to dose-blinding, we report combined dose group results. In the safety analysis, deucrictibant IR capsule was well tolerated with no treatment-related treatment emergent adverse events (TEAEs) and no TEAEs leading to treatment discontinuation. As measured using the Patient Global Impression of Change (PGI-C), the median (95% CIs) time to onset of symptom relief was 1.1 hours (1.0–1.2) and to substantial symptom relief was 2.7 hours (2.1–2.9). Substantial symptom relief was achieved by 12 hours in 96.2% of attacks. Using the PGI of Severity (PGI-S), the median time to attack severity reduction was 2.6 hours (2.0–2.9) and to complete attack resolution was 11.5 hours (11.0–13.0). Complete resolution within 24 hours was achieved in 85.8% of attacks, with 90.2% of these attacks achieving resolution with a single dose of deucrictibant IR capsule. Rescue medication was used in 4/265 (1.5%) attacks after deucrictibant.

Conclusions: Results of the ongoing RAPIDe-2 extension study provide further evidence on the long-term safety and efficacy of deucrictibant IR capsule for on-demand treatment of repeat HAE attacks.

Funding: AllerVie

F7

Impact of Body Mass Index on Response to Omalizumab in Patients with Chronic Spontaneous Urticaria

Giselle Mosnaim, MD; Michael Holden, MD; Benjamin Trzaskoma, MS; Sarbjit Saini, MD

Introduction: Omalizumab, an anti-immunoglobulin E, is approved for the treatment of chronic spontaneous urticaria (CSU); however, the impact of baseline body mass index (BMI) on treatment effect has not been fully explored.

Methods: A post-hoc analysis of pooled phase 3 ASTERIA I/II trials (NCT01287117/01292473) was conducted. Patients with H1-antihistamine-refractory CSU received omalizumab 300mg or placebo for up to 24 weeks. Change from baseline (CFB) to week 12 in weekly Itch Severity Score (ISS7) and weekly Urticaria Activity Score (UAS7) were determined, and least square means (LSM) were presented, stratified by BMI category (<25kg/m^2, ≥25–<30kg/m^2, and ≥30kg/m^2; n=45–61). Interaction tests were performed to assess the potential for non-homogeneity across BMI subgroups.

Results: Patients who received omalizumab 300mg had a greater improvement at week 12 in itch severity and disease activity versus placebo, regardless of BMI subgroup. For CFB to week 12 in ISS7, there was no significant difference (P=0.9124) across BMI subgroups: BMI <25kg/m^2, LSM = –10.37 for omalizumab vs –5.55 for placebo; BMI ≥25–<30kg/m^2, LSM = –10.82 for omalizumab vs –5.30 for placebo; BMI ≥30kg/m^2, LSM = –10.16 for omalizumab vs –4.93 for placebo. For CFB to week 12 in UAS7, there was no significant difference (P=0.9546) across BMI subgroups: BMI <25kg/m^2, LSM = –23.51 for omalizumab vs –12.02 for placebo; BMI ≥25–<30kg/m^2, LSM = –23.61 for omalizumab vs –11.28 for placebo; BMI ≥30kg/m^2, LSM = –22.31 for omalizumab vs –9.86 for placebo. Overall safety results for ASTERIA I/II have been previously published: Maurer NEJM 2013;368:924-35 and Saini JID 2015;135;67-75.

Conclusions: In patients with CSU, BMI did not appear to affect response to omalizumab. These data further highlight that omalizumab improves outcomes in a broad range of patients with CSU.

Funding: Genentech, Inc., a member of the Roche Group.

F8

Impact of Baseline Biomarkers on Response to Omalizumab in Patients with Chronic Spontaneous Urticaria

Giselle Mosnaim, MD; Michael Holden, MD; Benjamin Trzaskoma, MS; Jonathan A. Bernstein, MD

Introduction: Omalizumab, an anti-immunoglobulin E (IgE), is approved for the treatment of chronic spontaneous urticaria (CSU). Here, we investigated the impact of baseline biomarkers on response to omalizumab in patients with CSU.

Methods: We conducted a post-hoc analysis of pooled phase 3 ASTERIA I/II trials (NCT01287117/01292473). Patients with H1-antihistamine-refractory CSU received omalizumab 300mg (guideline-recommended initial dose) or placebo for up to 24 weeks. The proportion of patients with a response to omalizumab at week 12, defined as Urticaria Activity Score (UAS7)≤6, was analyzed. Patients were stratified by baseline IgE (≤40IU/mL vs >40IU/mL), chronic urticaria (CU) index (positive vs negative), and basophil numbers via blood histamine content (BHC; ≤8ng/mL vs >8ng/mL). To assess the potential for differential treatment effects by baseline status, interaction tests between treatment effect and the respective baseline biomarker variable were performed.

Results: The proportion of patients with a response to omalizumab at week 12 was greater for omalizumab vs placebo, regardless of baseline biomarker levels. For IgE ≤40IU/mL, 62.2% (n=28/45) of patients on omalizumab had UAS7≤6 vs 16.3% (n=7/43) for placebo; IgE >40IU/mL, 63.8% (n=60/94) vs 19.3% (n=17/88); interaction P=0.7298. For positive CU index, 50.0% (n=17/34) of patients on omalizumab had UAS7≤6 vs 7.7% (n=3/39) for placebo; negative CU index, 67.9% (n=76/112) vs 22.3% (n=21/94); interaction P=0.2441. For BHC ≤8ng/mL, 52.4% (n=11/21) of patients on omalizumab had UAS7≤6 vs 0% (n=0/20) for placebo; BHC >8ng/mL, 63.2% (n=48/76) vs 21.9% (n=16/73); interaction P=not calculable. Overall safety results for ASTERIA I/II have been previously published: Maurer NEJM 2013;368:924-35; Saini JID 2015;135;67-75.

Conclusions: Baseline biomarkers (IgE level, CU index, basophil numbers) did not appear to predict response to omalizumab in patients with CSU. Omalizumab appeared to have efficacy across several subgroups, irrespective of the biomarkers studied.

Funding: Genentech, Inc., a member of the Roche Group.

F9

Efficacy and Safety of Long-term Epicutaneous Immunotherapy in Peanut-allergic Children Aged 4 Through 7 Years in the Phase 3 PEOPLE Trial

David M. Fleischer MD, Sharon Chinthrajah MD, Stephanie Leonard MD, Katharine J. Bee PhD, Timothée Bois MS, Hugh A. Sampson MD

Introduction: The 12-month phase 3 PEPITES trial demonstrated epicutaneous immunotherapy (EPIT) with the VIASKIN® peanut patch containing 250 µg peanut protein (VP250) was statistically superior to placebo in desensitizing peanut-allergic children aged 4-11 years, with greater responder rates in younger children (aged 4-7 years). Here, we report efficacy and safety results among the 4-7-year-old subgroup after 3 years of treatment during the PEPITES open-label extension (OLE) study, PEOPLE.

Methods: Following PEPITES, eligible participants could receive VP250 for up to 36 months in PEOPLE or up to 60 months in the PEOPLE Extension study. In PEOPLE, double-blind, placebo-controlled food challenges (DBPCFCs) were performed at Month 12 (M12) and M36. Available efficacy outcomes were analyzed within the age subgroup of 4-7 years among participants enrolled in PEOPLE who were initially randomized to active treatment. Safety was assessed throughout the study according to frequency, severity, and relatedness of adverse events (AEs).

Results: Of PEPITES participants (N=356), 298 enrolled in PEOPLE, of which 161 (54%) were aged 4-7 years at treatment initiation in PEPITES, and 103 were randomized to active treatment. Among this age subgroup, treatment responder rates increased from 44.7% at M12 to 60.5% at M36, with increases also observed in the proportion of participants achieving an ED ≥ 1000 mg (M12: 39.8%, M36: 55.0%), and the proportion consuming a cumulative dose of 3444 mg (equivalent to 12-14 peanuts) without meeting stopping criteria (M12: 6.8%, M36 23.8%). Safety assessments were consistent with previously published findings in the overall age group.

Conclusions: Among children aged 4-7 years at PEPITES entry, treatment with VP250 showed continued increases in treatment effect with a consistently favorable safety profile out to 36 months. These data support the potential of VP250 as a long-term treatment option for peanut-allergic children, if approved.

Funding: DBV Technologies

F10

Correlating Changes in Skin Clearance/Clinical Reported Outcomes with Patient Reported Outcome Measures in Atopic Dermatitis

Kathryn Smiley, PA-C; Nicole Navasero, BS; Anoushka Tambay, BS; Lauren Galli, BS; Bob Geng, MD

Introduction: Clinician-reported outcomes (CROs) such as Eczema Area Severity Index (EASI), Body Surface Area (BSA), and Validated Investigator Global Assessment (vIGA) are validated atopic dermatitis (AD) assessments but may not fully reflect patients' lived experiences. Patient-reported outcomes (PROs) like itch scores, POEM (Patient-Oriented Eczema Measure), and quality of life scales (CDLQI, DLQI) capture subjective burden. This study evaluates correlations between CROs and PROs to identify gaps in disease assessment.

Methods: This interim analysis includes retrospective and prospective data from 50 patients with moderate to severe AD (baseline vIGA 3 or 4) from two clinics. Eligible patients completed at least two visits. CROs (EASI, BSA, vIGA) and PROs (itch NRS, POEM, CDLQI and NEA questionaries) were analyzed using Spearman's correlation. Correlations of mean differences and stratified disease severity subgroup analyses (ex. EASI50/75/90, vIGA 0/1, BSA <10%) were also evaluated.

Results: Strongest overall correlations were between EASI and itch NRS ($\rho = 0.704$, $p < 0.0001$). Mean EASI and mean itch NRS also correlated significantly ($\rho = 0.656$, $p < 0.0001$). In patients with BSA <10%, BSA and itch NRS showed strong correlations ($\rho = 0.529$, $p < 0.0001$). Weaker associations emerged between CROs and CDLQI or POEM subscales, especially in quality-of-life domains. Notably, EASI and CDLQI friendships showed a weak correlation ($\rho = 0.194$, $p = 0.0078$), and several vIGA 0 comparisons could not be computed due to limited variability.

Conclusion: CROs like EASI and BSA show strong correlations with itch, particularly in patients showing improvement. However, weaker links with quality-of-life measures suggest CROs alone may not capture the full disease burden. These findings highlight the importance of integrating PROs into routine assessment. Further studies with larger cohorts are needed to explore weakly correlated metrics and improve holistic evaluation of AD burden.

Funding: Eli Lilly and Company

F11

Understanding the Impact of Long-Term Prophylaxis Switches for Patients With Hereditary Angioedema

Steve Dorman, MD, Donald L. McNeil, MD, Jean A. Nelson, MD, John Anderson, MD, Lucy Howard, BSc, Tom Bailey, MSc, Edna Mugwagwa, MSc, Daniel Fox, PharmD, MBA, Krystal Sing, PharmD, Bob G. Schultz, PharmD, BS, Salomé Juethner, MSN, RN

Introduction: Data reporting the impact of long-term prophylaxis (LTP) switches on disease management and patient-reported outcomes (PROs) among patients with hereditary angioedema (HAE) are limited.

Methods: Patients with HAE aged >18 years in the US who initiated lanadelumab LTP before switching to berotralstat then back to lanadelumab were eligible and enrolled through centers that completed a linked chart-review, or directly through a patient research register. Clinical and PRO data were collected.

Results: This interim analysis included 15 patients (mean±SD age 46.5±14.3 years; 100% female; 80.0% HAE Type I/II). Mean±SD time on each treatment cycle was 31.2±15.7, 5.6±4.8, and 23.3±14.8 months (lanadelumab>berotralstat>lanadelumab). Reasons for discontinuing first-cycle lanadelumab included preferred different route of administration (53.3%) and clinical trial enrolment (20.0%); no patients discontinued due to lack of effectiveness. Reasons for berotralstat discontinuation included poor tolerability (40.0%), lack of attack prevention (26.7%), lack of effectiveness (26.7%), and patient request (20.0%). During first-cycle lanadelumab, 13.3% experienced severe attacks and none experienced life-threatening attacks. No patients experienced severe or life-threatening attacks during second-cycle lanadelumab. While using berotralstat, 26.7% experienced severe and 6.7% experienced life-threatening attacks. On both lanadelumab cycles, 46.7% reported complete treatment satisfaction, whereas no patients were completely satisfied with berotralstat.

Conclusion: In this interim analysis of an ongoing study, patients who switched from lanadelumab>berotralstat>lanadelumab reported lack of effectiveness and attack prevention as reasons for switching back to lanadelumab. Almost half of patients reported complete satisfaction with lanadelumab. Given selection criteria and small sample, findings may not be generalizable to all patients with HAE.

Funding: Takeda Pharmaceuticals USA, Inc.

F12

Lanadelumab's sustained effectiveness and safety for HAE long-term prophylaxis in patients from Puerto Rico: Final results from the EMPOWER Study

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Introduction: The Phase 4, observational, multiregional EMPOWER Study (NCT03845400) prospectively evaluated the effectiveness and safety of lanadelumab for long-term prophylaxis in patients with hereditary angioedema (HAE) for up to 3 years. Here, we report final study data in patients from Puerto Rico.

Methods: Enrolled patients with HAE-C1INH who initiated lanadelumab treatment were classified as new or established according to lanadelumab doses received pre-enrollment (<4 or ≥4, respectively). Lanadelumab exposure data were captured by electronic case report forms. Effectiveness was assessed by change in HAE attack rate before versus after lanadelumab initiation. Safety was assessed through treatment-emergent adverse events (TEAEs).

Results: Nine patients (1 new [lanadelumab-naïve pre-enrollment], 8 established) aged 36–73 years enrolled at the Puerto Rican site. All patients were of Hispanic/Latino ethnicity (White: 66.7%; female: 77.8%; HAE-C1INH-Type1: 55.6%), and most (n=8/9) received lanadelumab 300 mg every 2 weeks; 1 established patient received every-4-weeks dosing. Lanadelumab exposure ranged from approximately 2.3 years for the new patient to >2.5 years in most established patients. At the end of study, treatment was ongoing in 7 (78%) patients; 2 patients discontinued treatment (n=1, reimbursement/insurance-related access issues; n=1, mild fatigue). In the new patient, physician-reported HAE attack rate reduced by 76% from 1.99 attacks/month before to 0.47 attacks/month after lanadelumab initiation; most attacks were mild (15.4%) or moderate (61.5%). For established patients, mean (95% confidence interval) observed physician-reported HAE attack rate was 0.26 (0.09–0.42) attacks/month; most attacks were mild (24.1%) or moderate (57.5%). Two patients were attack-free on treatment. In total, 5 TEAEs occurred in 4 patients, none of which were serious or fatal. One patient experienced treatment-related mild fatigue.

Conclusions: Findings from this analysis support the clinical benefits and safety of lanadelumab treatment for HAE prophylaxis in patients from Puerto Rico.

Funding: Takeda Development Center Americas, Inc

F13

Matched-Adjusted Indirect Comparison Analysis Demonstrating Significantly Better Improvement in Patient-Reported Outcomes for Omalizumab Versus Dupilumab at 12 Weeks in Patients with Chronic Spontaneous Urticaria

Giselle Mosnaim, MD, Arpamas Seetasith, PhD; Benjamin Trzaskoma, MS; Michael Holden, MD, Sarbjit Saini, MD

Introduction: Given head-to-head randomized clinical trials are not available for omalizumab versus newer treatments for chronic spontaneous urticaria (CSU), we used matched-adjusted indirect comparison analysis to assess efficacy of omalizumab versus dupilumab.

Methods: We analyzed data from the pooled omalizumab ASTERIA I/II trials (NCT01287117/01292473) and compared with published summary data from the dupilumab LIBERTY-CSU CUPID Study A trial (NCT04180488) to assess change from baseline (CFB) at week 12 in weekly itch severity score (ISS7) and weekly urticaria activity score (UAS7). Patients in ASTERIA were matched to available data from LIBERTY-CSU using distribution of baseline UAS7<28 (29.7% of patients) and UAS7≥28 (70.3%): random samples from ASTERIA (N=1000) were drawn without replacement to match the comparator distributions within treatment arms. Outcomes for omalizumab 300mg versus dupilumab standard-dose were compared using two-sample t-tests. Analysis limitations: different background treatment, different primary outcomes, availability of published data.

Results: Indirect comparisons of CFB in ISS7 and UAS7 at week 12 showed significantly greater improvements with omalizumab compared with dupilumab. For CFB in ISS7, the least squares mean (LSM) difference (95%CI) between treatment and placebo was -5.4(-6.9, -4.0) for omalizumab and -2.4(-4.6, -0.1) for dupilumab: omalizumab versus dupilumab = -3.0(-5.8, -0.3), P=0.031. For CFB in UAS7, the LSM difference (95%CI) between treatment and placebo was -12.6(-15.7, -9.5) for omalizumab and -5.0(-9.3, -0.7) for dupilumab: omalizumab versus dupilumab = -7.6(-13.0, -2.2), P=0.006. Safety results published: ASTERIA I/II - Maurer NEJM 2013;368:924-35, Saini JID 2015;135;67-75; CUPID Study A - Maurer JACI 2024;154:184-194.

Conclusions: In patients with CSU, omalizumab demonstrated superior efficacy versus dupilumab: using matched-adjusted indirect comparison analyses, improvements in itch severity and disease activity were greater at week 12. These data highlight that omalizumab remains an effective and superior treatment option for patients with CSU.

Funding: Genentech, Inc., a member of the Roche Group.

F14

Identification of Chronic Spontaneous Urticaria within Electronic Health Record using Machine Learning Algorithms

Shruti Sehgal*, MD(Hom.), MS, Chengsheng Mao*, PhD, Lucy A. Bilaver, PhD, Sai Nimmagadda, MD, PhD, Ruchi Gupta, MD, MPH, Yuan Luo, PhD

Introduction: Chronic Spontaneous Urticaria (CSU) affects 0.5-1% of the population worldwide, often impacting quality of life. Medications for treatment include H1 antihistamines, and anti-IgE omalizumab for unresponsive patients. The overarching goal of this project is to identify clusters of CSU patients exhibiting distinct phenotypic characteristics that can point to differences in disease condition and response to treatments. As an initial step, we utilized Electronic Health Record (EHR) data to identify patients with CSU using machine learning (ML) algorithms.

Methods: We identified a cohort of patients from the Northwestern Medicine Enterprise Data Warehouse with ICD codes L50, T78.3, T78.3XXA, T78.3XXD, T78.3XXS, or diagnosis name containing 'urticaria' and 'chronic'. Additionally, patients were required to have ≥2 outpatient visits ≥6 weeks apart, or one outpatient visit and a diagnostic name of chronic urticaria. Patients were identified as having CSU if "chronic spontaneous urticaria/CSU" or "chronic idiopathic urticaria/CIU" was documented within the clinical notes. Structured data, such as labs, medications, vital signs, comorbidities, and demographics were used for CSU prediction. Three machine learning algorithms were applied: Logistic Regression (LR), XGBoost (XGB), and Random Forest (RF). Metrics for model performance were Area Under the Curve (AUC), sensitivity, and specificity.

Results: We had 14777 patients and 2300 identified as having CSU/CIU. The ML approaches utilized 158 features for prediction. LR showed highest sensitivity (0.65) with an AUC of 0.71, XGB achieved highest specificity (0.80) and an AUC of 0.76, while RF demonstrated a balanced trade-off between sensitivity (0.61) and specificity (0.74) with an AUC of 0.76.

Conclusions: Our findings suggest that ML classifiers are effective for identifying patients with CSU from structured EHR data. Next, large language models and self-supervised learning can be leveraged to evaluate common characteristics and variations among CSU patients, potentially offering clinicians a more holistic way to examine CSU complexity and improve clinical outcomes.

Funding: Genentech (Award # SL45290)

F15

Long-Term Safety and Efficacy of Oral Deucrictibant for Prophylaxis in Hereditary Angioedema: Data Snapshot Results of the CHAPTER-1 Open-Label Extension (OLE) Study

John Anderson M.D., Michael E. Manning M.D., H. James Wedner M.D., Peng Lu M.D., Ph.D., Marc A. Riedl M.D.

Introduction: Deucrictibant is a selective, orally administered bradykinin B2 receptor antagonist under development for prophylactic and on-demand treatment of hereditary angioedema (HAE) attacks. The two-part, Phase 2 CHAPTER-1 study (NCT05047185) evaluates the efficacy and safety of deucrictibant for long-term prophylaxis of HAE attacks.

Methods: CHAPTER-1 enrolled 34 participants who were aged ≥18 and ≤75 years, diagnosed with HAE-1/2, and had experienced either ≥3 attacks within 3 months prior to screening or ≥2 attacks during screening (up to 8 weeks). Thirty participants completed part 1, during which they received deucrictibant 20 mg/day (n=11), 40 mg/day (n=10), or placebo (n=9) for 12 weeks. All thirty participants continued into the OLE and received treatment with deucrictibant 40 mg/day.

Results: This data snapshot (cutoff: 10 June 2024) included 30 participants who received deucrictibant 40 mg/day for a mean duration of 12.8 months (maximum ~20 months) in the OLE. The safety analysis showed no treatment-related serious treatment emergent adverse events (TEAEs), no TEAEs leading to study drug discontinuation, and that deucrictibant was well tolerated. At study baseline, participants had a mean (standard deviation) attack rate of 2.18 (1.35) and a least squares mean (LSM) attack rate of 0.15 (standard error [SE] 0.05) in the OLE. Attack rate in the OLE was low irrespective of participants' attack rate at study baseline: 0.10 and 0.19 for participants with ≥1 to <2 attacks/month and ≥2 attacks/month at study baseline, respectively. During the OLE, the LSM (SE) rates of "moderate and severe" attacks and attacks treated with on-demand medication were 0.07 (0.03) and 0.07 (0.02), respectively. The median proportion of days with HAE symptoms in the OLE was 0.0%.

Conclusions: Results from the ongoing CHAPTER-1 OLE extend the part 1 findings and provide additional evidence on the long-term safety and efficacy of deucrictibant treatment for prophylaxis of HAE attacks.

Funding: AllerVie

F16

Design of a Phase 4, Prospective, Observational, Multicenter Registry to Assess Baseline Characteristics, Treatment Patterns, and Long-term Outcomes in Patients With Eosinophilic Esophagitis Initiating Dupilumab in Routine Clinical Practice

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Introduction: Dupilumab, a fully human monoclonal antibody that blocks key drivers of type 2 inflammation, has been approved in the USA and EU for the treatment of eosinophilic esophagitis (EoE) in patients≥1 year weighing ≥15 kg, based on the results of randomized controlled trials. However, data on the use of dupilumab for EoE in real-world clinical practice are limited. Here we present the design of a phase 4, prospective, observational, multicenter registry (EDESIA; Evaluation of Dupilumab for Eosinophilic Esophagitis: Registry Study in Adults and Adolescents) that aims to investigate the effect of dupilumab use for EoE in routine clinical practice in the USA.

Methods: Patients ≥12 years with EoE who initiate dupilumab treatment according to FDA-approved prescribing information will be eligible for enrollment. Eligible patients must be willing and able to comply with the required registry procedures and assessments, able to understand and complete registry-related questionnaires, and provide written, informed consent. Exclusion criteria include a contraindication to dupilumab per the prescribing information; treatment with dupilumab within 6 months prior to the screening assessment; any condition that, in the opinion of the investigator, may interfere with the patient's ability to participate in the registry; or participation in an ongoing interventional study within 6 months of the baseline assessment. Patients will be assessed at baseline, Months 3 and 6, and every 6 months through Month 36. Target enrollment is 300 patients.

Results: EDESIA will assess baseline demographic and disease characteristics and treatment patterns (including concomitant medications) and generate longer-term real-world safety and effectiveness data in patients with EoE initiating dupilumab treatment in clinical practice.

Conclusions: The results of EDESIA will expand on prior clinical trials by collecting data on demographic and disease characteristics, treatment patterns, and outcomes among patients ≥12 years receiving dupilumab for the treatment of EoE in a real-world setting.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F17

Dupilumab Effectiveness Through Two Years in Patients with CRSwNP Treated in Real-World Practice: Results from the Global AROMA Registry

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Introduction: Chronic rhinosinusitis with nasal polyps (CRSwNP) has a high symptom burden and severely impacts health-related quality of life. Dupilumab significantly reduced symptoms in clinical trials, but evidence in real-world practice is limited.

Methods: AROMA (NCT04959448) is a phase 4, prospective, global registry study of adults with CRSwNP initiating dupilumab in real-world practice in the USA, Canada, Germany, Italy, Japan, and the Netherlands.

Results: 691 patients initiated dupilumab; median age 53 years (IQR 42–61), 55.7% male, 69.5% White, 69.2% with asthma, 74.1% with prior sinonasal surgery. Overall, 40.7% had been prescribed antibiotics for CRSwNP and in the 2 years prior to dupilumab initiation, 65.8% were prescribed systemic corticosteroids for CRSwNP. Nasal congestion score (range 0–3) decreased from mean 1.8 (SD 0.86) at baseline to 0.9 (0.75) at Month 3 (M3), 0.7 (0.74) at M12, and 0.5 (0.66) at M24. Similar improvements were seen with loss of smell score (range 0–3): mean (SD) 2.2 (1.06), 1.2 (1.04), 1.0 (1.02), and 0.9 (0.96) at baseline, M3, M12, and M24, respectively, and SNOT-22 (range 0–110): 45.9 (21.37), 21.3 (15.67), 17.0 (14.31), 18.4 (14.55). The proportions of patients reporting "no symptoms" (patient global assessment of symptom severity) increased from 3.3% at baseline to 32.6% and 42.9% at M12 and M24, respectively. Safety was consistent with the known safety profile of dupilumab.

Conclusions: In the AROMA global CRSwNP registry, dupilumab rapidly improved symptoms and health-related quality of life with continued improvements through 24 months' follow-up. These results support dupilumab's long-term effectiveness in CRSwNP in real-world clinical practice.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F18

Ultra-sensitive testing identifies previously undetected *KIT* D816V mutations in patients with indolent systemic mastocytosis: Learnings from the PIONEER study of avapritinib

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Introduction: Indolent systemic mastocytosis (ISM) is characterized by long-term, debilitating cutaneous, gastrointestinal, neurological, and musculoskeletal symptoms. ISM is a clonal mast cell (MC) disease primarily driven by a *KIT* D816V mutation. This mutation can be difficult to detect in the peripheral blood (PB) of patients with ISM and low MC burden, even with the current gold standard test (droplet digital PCR, ddPCR), leading to diagnostic delays. More sensitive assays are needed to help physicians identify patients with D816V-mutant *KIT* and underlying clonal MC disorders, including ISM. Super rolling circle amplification (superRCA) is an assay in development with ~30-fold greater sensitivity for *KIT* D816V detection *versus* ddPCR.
Using samples from PIONEER (NCT03731260), which demonstrated that avapritinib (a KIT D816V inhibitor) effectively reduces symptoms and MC burden in ISM, we investigated whether superRCA could detect *KIT* D816V in patients without detectable mutations by ddPCR.

Methods: All patients enrolled in PIONEER met ISM diagnostic criteria, confirmed by central pathology review. During screening, PB from all patients was tested for mutant-*KIT* D816V by ddPCR; those without detectable mutations were retrospectively tested by superRCA.

Results: In combination, superRCA and ddPCR detected *KIT* D816V mutations in PB of 238/246 (97%) of patients. *KIT* D816V was detected in 209/246 (85%) PB samples tested by ddPCR. In 37 samples without detectable *KIT* D816V by ddPCR, superRCA detected *KIT* D816V in 29. Baseline chronic total symptom scores per the ISM-Symptom Assessment Form (©2018 Blueprint Medicines Corporation) were similar in patients with ddPCR-detected versus superRCA-detected *KIT* D816V.

Conclusion: SuperRCA detected *KIT* D816V in patients with ISM without detectable *KIT* D816V by ddPCR. SuperRCA increased sensitivity limits for mutant-*KIT* D816V in PB and would facilitate the diagnosis of ISM in patients without detectable *KIT* D816V by currently available tests. Further development of superRCA may improve the detection of clonal MC disorders.

Funding: Blueprint Medicines Corporation.

F19

Long-Terms Effects of Avapritinib on Bone Health and Quality of Life in Patients With Indolent Systemic Mastocytosis: Analysis of the PIONEER Study

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Introduction: Indolent systemic mastocytosis (ISM) is a clonal mast cell disease, primarily driven by the *KIT* D816V mutation, often characterized by debilitating cutaneous, gastrointestinal, and musculoskeletal symptoms as well as comorbid conditions of osteoporosis or osteopenia. Avapritinib, a selective KIT D816V inhibitor, is approved for ISM at 25 mg once daily (QD).

Methods: Patients with moderate-to-severe ISM, uncontrolled despite best supportive care (BSC), enrolled in PIONEER (NCT03731260) and were eligible to receive avapritinib+BSC in the open-label extension. Dual-energy X-ray absorptiometry (DXA) scans were optional. Bone mineral density (BMD) data were retrospectively collected at a single site with uniform serial DXA scans. Symptom burden and quality of life (QoL) were assessed using the ISM-Symptom Assessment Form (©2018 Blueprint Medicines Corporation) total symptom score (TSS) and Mastocytosis Quality of Life Questionnaire (MC-QoL). Safety was assessed.

Results: Impact on BMD: Across all patients enrolled in PIONEER, 48/251 (19%) had osteopenia or 56/251 (22%) osteoporosis at baseline. Thirteen patients at a single site with DXA scans showed improved BMD after 2 years of avapritinib: mean BMD increased 4.79%±4.78% (lumbar spine) and 2.30%±6.46% (femoral neck).
Long-Term Follow-Up:
226 patients initiated avapritinib 25 mg QD with median follow-up of 3 years. Patients had durable improvement in TSS from baseline to Week 96 and 144 (mean change –17.51 and
–20.07, respectively) and in MC-QoL. Long-term follow-up showed avapritinib was generally well tolerated with no new safety concerns.

Conclusions: Osteoporosis and osteopenia are prominent features in ISM and the PIONEER population. The positive impact of avapritinib on bone health provides motivation for prospective studies assessing BMD in ISM. Avapritinib demonstrated durable improvements in disease symptoms and QoL after a median follow-up of ~3 years. Avapritinib is an effective and generally well tolerated therapeutic option with a favorable long-term benefit-risk profile.

Funding: Blueprint Medicines Corporation.

F20

Rationale and design of the Garadacimab REAl-world Treatment outcomes of effectiveness, safety and quality-of-life in patients with hereditary angioedema (GREAT) study

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Background: Garadacimab (anti-activated factor XII antibody) has demonstrated early and durable efficacy with a favorable long-term safety profile in the Phase 2, pivotal Phase 3 (VANGUARD) and ongoing Phase 3 open-label extension studies in patients with hereditary angioedema (HAE). In 2025, garadacimab was approved for use as once-monthly long-term prophylaxis (LTP) in patients with HAE in Europe, the UK, Australia and Japan. Real-world data provide insights from routine clinical practice and can be used to inform treatment decisions in HAE. The GREAT study will investigate long-term effectiveness, safety, health-related quality of life (HRQoL) and healthcare resource utilization (HCRU) outcomes in patients with HAE receiving garadacimab LTP in the real-world setting.

Methods: This prospective, noninterventional, observational cohort study will enroll patients aged ≥12 years with physician- and laboratory-confirmed HAE newly initiating on-label garadacimab (200 mg subcutaneous once monthly) from ~30 centres in Europe, the UK, North America and the Asia-Pacific region (target enrollment: 200 patients). Participants will be observed on treatment for a target duration of 24 months with a 30-day follow-up period. The GREAT study will evaluate the characteristics of the enrolled population, HAE attack rate (on treatment with garadacimab vs pre-enrollment baseline), time to occurrence of first HAE attack, the proportion of patients achieving attack-free status, and attack-free duration. It will assess safety, HRQoL, productivity, treatment patterns, HCRU and the economic impact of garadacimab LTP, treatment adherence and satisfaction, and patient preference. Retrospective data on HAE attacks and treatments, and on HCRU will be collected from 12 months prior to garadacimab initiation.

Results: The study will begin to enroll patients in mid-2025 and is estimated to complete in 2029.

Conclusions: The GREAT study will provide the first comprehensive real-world evidence on the use of garadacimab as LTP against HAE.

Funding: CSL Behring LLC

F21

Efficacy And Safety of Garadacimab Via Autoinjector/Pre-Filled Pen for Hereditary Angioedema Long-Term Prophylaxis – Interim Results From A Phase 3 Open-Label Extension Study

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Background: Garadacimab (anti-activated factor XII antibody) administered subcutaneously (SC) once-monthly via needle-safety device (NSD) demonstrated durable protection against hereditary angioedema (HAE) attacks with favorable long-term safety/tolerability profiles across clinical studies. Administration via autoinjector/pre-filled pen (AI/PFP) may offer increased convenience. We report efficacy and safety in patients with HAE receiving garadacimab as long-term prophylaxis via AI/PFP from the ongoing Phase 3 open-label extension study (OLE; NCT04739059).

Methods: In the OLE, patients who received garadacimab 200 mg SC once-monthly via NSD for ≥12 months transitioned to garadacimab administration via AI/PFP. Post hoc efficacy and safety analyses for garadacimab administration via AI/PFP from device transition (NSD to AI/PFP) through to data cutoff (July 9, 2024) are presented.

Results: Overall, 136 patients received garadacimab via AI/PFP for a median (range) of 9.4 (2.7–12.6) months (total exposure: 104.3 patient years); of these, 129 (95%) patients were treated for ≥6 months. The mean monthly attack rate (standard deviation) was 0.08 (0.25). Fifty-eight (43%) patients experienced ≥1 treatment-emergent adverse event (TEAE), totaling 173 TEAEs. Of these, six TEAEs were garadacimab-related injection-site reactions which occurred in 3 patients (2%), all mild in severity. No TEAEs led to death/discontinuation. Most TEAEs were mild or moderate (166/173, 96%). There were 3 serious adverse events (food allergy, fractured fingers, fractured skull; n=1 each), none were garadacimab-related. No adverse events of special interest per protocol (thromboembolic/abnormal bleeding events, severe hypersensitivity/anaphylaxis) were observed.

Conclusion: Long-term prophylaxis with garadacimab administered via AI/PFP showed durable protection against HAE attacks along with a favorable safety profile.

Funding: CSL Behring, LLC.

F22

Long-Term Efficacy Of Garadacimab For Hereditary Angioedema In Patients With Or Without Prior Exposure In A Phase 3 Open-Label Extension Study

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Background: Garadacimab (anti-activated factor XII monoclonal antibody) 200 mg subcutaneously once monthly demonstrated durable efficacy and a favorable long-term safety profile for hereditary angioedema (HAE) prophylaxis in an ongoing Phase 3 open-label extension (OLE) study (NCT04739059). Efficacy was previously reported, per protocol, for rollovers from prior studies (received either garadacimab or placebo) and newly enrolled patients. This post hoc analysis reports efficacy for patients with prior garadacimab exposure (received garadacimab in prior study) and garadacimab-naïve patients (received placebo in prior study or newly enrolled).

Methods: All patients were stratified post hoc into prior garadacimab exposure and garadacimab-naïve cohorts. Mean monthly attack rates and reduction vs run-in were assessed at data cut-off (February 13, 2023) and for 3-month treatment windows across the OLE.

Results: Median (interquartile range) garadacimab exposure was 21.9 months (17.7–37.4) for patients with prior garadacimab exposure (n=71), and 13.3 months (12.2–14.4) for garadacimab-naïve patients (n=90).
Mean (standard deviation, SD) monthly attack rate was 0.1 (0.3) for patients with prior garadacimab exposure and 0.2 (0.4) for garadacimab-naïve patients, corresponding to 96.8% and 93.0% reductions vs run-in, respectively. Mean (SD) monthly attack rate was reduced by 96.3% (12.1) and 91.5% (19.0) in Months 1–3 vs run-in, and ≥90% reductions were observed for each 3-month treatment window in both cohorts. Most patients were attack-free (66.2% [n=47] with prior garadacimab exposure and 54.4% [n=49] garadacimab-naïve patients).

Conclusions: Long-term prophylaxis with garadacimab provided durable protection against HAE attacks throughout the OLE in patients with prior garadacimab exposure and garadacimab-naïve patients, consistent with previous findings.

Funding: CSL Behring, LLC.

F23

Baseline Characteristics Associated With Multicomponent Clinical Remission Following Dupilumab Treatment In Patients With Moderate-To-Severe Asthma

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Introduction: This post hoc analysis aimed to identify baseline characteristics associated with achieving on-treatment clinical remission in patients with moderate-to-severe asthma receiving dupilumab or placebo who completed QUEST (NCT02414854).

Methods: In QUEST, patients received either add-on dupilumab 200/300 mg or placebo every two weeks for 52 weeks. Remission was defined as meeting all the following criteria at QUEST Week 52: no exacerbations, no oral corticosteroid use, stable (decrease in pre- or post-bronchodilator forced expiratory volume in 1 second [FEV_1] <5% from baseline) or improved lung function, and 5-item Asthma Control Questionnaire score <1.5.

Results: At QUEST Week 52, 38.3% of dupilumab recipients (n=387) and 26.2% of placebo recipients (n=136) achieved clinical remission. In patients receiving dupilumab vs placebo, the likelihood of achieving remission at QUEST Week 52 was significantly higher when baseline blood eosinophil counts were ≥150, ≥300, or ≥500 cells/µL (OR [95% CI] 2.17 [1.64, 2.86]; 2.74 [1.92, 3.92]; 4.04 [2.45, 6.68], respectively; all P<0.0001) but not <150 cells/µL. The likelihood of achieving remission was significantly higher for dupilumab vs placebo in patients with baseline fractional exhaled nitric oxide [FeNO] levels ≥20 and ≥50 ppb (2.35 [1.74, 3.16], P<0.0001; 2.26 [1.38, 3.70], P<0.01, respectively) but not <20 ppb. Patients receiving dupilumab vs placebo were likely to achieve remission irrespective of baseline pre-bronchodilator FEV_1 category: ≤1.75 L (1.90 [1.36, 2.66], P<0.001); >1.75 L (1.61 [1.15, 2.24], P<0.01).

Conclusions: In this patient population**,** elevated blood eosinophil counts and FeNO levels at baseline were both associated with a higher likelihood of achieving remission following dupilumab treatment.

Funding: Sanofi and Regeneron Pharmaceuticals Inc

F24

Dupilumab Treatment Significantly Reduces Age-associated Total IgE Levels in Young Children With Atopic Dermatitis

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Introduction and Objectives: Most patients with moderate-to-severe atopic dermatitis (AD) have elevated total immunoglobulin E (IgE), an allergen sensitization marker contributing to the pathophysiology of other atopic conditions like food allergies and asthma. In AD, IgE sensitization correlates with increased severity and flares, and atopic comorbidity development, especially in young children (atopic march). This analysis reports total IgE level differences at baseline and after dupilumab treatment in different age cohorts of 0.5 to <6-year-old children with moderate-to-severe AD.

Methods: In LIBERTY AD PRESCHOOL (NCT03346434), children with moderate-to-severe AD aged <6 years (yrs) received dupilumab or placebo, both with topical corticosteroids (TCS), for 16 weeks. Baseline and Week 16 total IgE levels are reported, stratified by age cohort: 0.5 to <2yrs, ≥2 to <4yrs, and ≥4 to <6yrs. Mixed-effect model for repeated measures was used to compare the IgE ratio and the difference between Week 16 and baseline.

Results: At baseline, mean IgE levels (kU/L) showed age-cohort–dependent increase in both dupilumab (n=71) and placebo (n=69) arms: 0.5 to <2yrs, 3,481.8 and 636.3; ≥2 to <4yrs, 5,736.4 and 5,066.7; ≥4 to <6yrs, 10,046.0 and 9,044.9, respectively. At Week 16, dupilumab+TCS vs placebo+TCS significantly reduced IgE levels in children aged 0.5 to <2yrs (275.9 vs 918.0), ≥2 to <4 yrs (1,233.3 vs 4,960.0), and ≥4 to <6 yrs (3,932.8 vs 9,510.4). Overall, mean IgE levels were significantly reduced by 70% in dupilumab+TCS arm (P<0.001), while increased by 30% in placebo+TCS arm, (P=0.03).

Conclusion: IgE levels increased with age in young children with moderate-to-severe AD on placebo+TCS. In contrast, dupilumab+TCS treatment significantly decreased IgE levels in all tested age cohorts. Given that total IgE progressively increases with increasing age in young children, early intervention with dupilumab in children with moderate-to-severe AD may contribute to lowering the risk of developing atopic comorbidities.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F25

Initiation of dupilumab led to reduced use of corticosteroids and antibiotics over 12 months in patients with chronic rhinosinusitis with nasal polyps treated in US real world practice

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Introduction: Dupilumab has demonstrated improvements in objective and patient-reported outcomes in patients with severe chronic rhinosinusitis with nasal polyps (CRSwNP) in randomized clinical trials and in real-world practice. There is currently limited evidence on dupilumab effectiveness in US clinical practice. This study aims to compare the burden of corticosteroid and antibiotic use in CRSwNP patients before and after initiation of dupilumab in the US.

Methods: A retrospective observational cohort study in adults with CRSwNP who initiated dupilumab 300 mg every 2 weeks between June 2019 and June 2022. Data from the OM1 Real-World Data Cloud, inclusive of claims and electronic health record data, and the Reg-ENT Registry were used. In this analysis, CRSwNP-related use of oral corticosteroids (OCS) was defined as within 5 days of a CRS and/or NP diagnosis or within 30 days of a sinus surgery. CRSwNP-related OCS use and prescription of intranasal corticosteroids (INCS) and antibiotics in the 12 months before and after initiation of dupilumab (pre- and post-dupilumab periods, respectively) are summarized descriptively.

Results: The overall cohort comprised 1016 patients. The proportion of patients with CRSwNP-related OCS use decreased from 59.1% in the pre-dupilumab period to 17.7% in the post-dupilumab period; 76.5% of patients with CRSwNP-related OCS use pre-dupilumab had no CRSwNP-related OCS use post-dupilumab. Among patients with comorbid asthma (n=579 [57.0%]), CRSwNP-related OCS use decreased from 58.7% (pre-dupilumab) to 18.7% (post-dupilumab). In the overall cohort, the use of INCS reduced from 50.5% to 31.1% and the use of antibiotics reduced from 64.6% to 31.8%.

Conclusions: Patients with CRSwNP who initiated dupilumab had reduced corticosteroid and antibiotic use during the 12 months following dupilumab initiation compared to the 12 months pre-dupilumab. These findings support the real-world effectiveness of dupilumab in reducing exacerbations in patients with CRSwNP in the US.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F26

Efficacy of tezepelumab in patients with severe, uncontrolled asthma grouped by median baseline serum IL-5 And IL-13 levels: Results from the phase 3 NAVIGATOR study

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Introduction: Interleukin (IL)-5 and IL-13 are common drivers of inflammation in severe asthma. In the phase 3 NAVIGATOR study (NCT03347279), tezepelumab reduced serum IL-5 and IL-13 levels and the annualized asthma exacerbation rate (AAER) in patients with severe, uncontrolled asthma. This *post hoc* analysis evaluated the AAER in NAVIGATOR participants grouped by baseline IL-5 and IL-13 levels.

Methods: NAVIGATOR was a multicenter, randomized, double-blind, placebo-controlled study. Patients (12-80 years old) with severe, uncontrolled asthma were randomized to tezepelumab 210 mg or placebo subcutaneously every 4 weeks for 52 weeks. The AAER was estimated for tezepelumab and placebo recipients grouped by ≥ or < median baseline serum IL-5 and IL-13 levels: IL-5-high/IL-13-high, IL-5-high/IL-13-low, IL-5-low/IL-13-high, IL-5-low/IL-13-low.

Results: Median baseline IL-5 and IL-13 levels were 0.86 pg/mL and 0.05 pg/mL, respectively. Most patients were IL-5-high/IL-13-high (tezepelumab, n=206; placebo, n=197) or IL-5-low/IL-13-low (tezepelumab, n=204; placebo, n=192); fewer patients were IL-5-high/IL-13-low (tezepelumab, n=51; placebo, n=57) or IL-5-low/IL-13-high (tezepelumab, n=52; placebo, n=60). Among placebo recipients, the AAER over 52 weeks was higher in IL-5-high/IL-13-high patients than in IL-5-low/IL-13-low patients (AAER [95% CI]: 2.54 [2.07, 3.12] vs 1.94 [1.57, 2.40], respectively). Tezepelumab demonstrated greater absolute and relative AAER reductions versus placebo in IL-5-high/IL-13-high patients (difference: −1.77 [−2.31, −1.23]; rate ratio: 0.30 [0.22, 0.41]) than in IL-5-low/IL-13-low patients (difference: −0.77 [−1.24, −0.29]; rate ratio: 0.61 [0.45, 0.82]).

Conclusions: Patients with severe, uncontrolled asthma with elevated serum IL-5 and IL-13 levels who received tezepelumab versus placebo had greater absolute and relative reductions in exacerbations than those without elevated levels.

Funding: AstraZeneca and Amgen Inc.

F27

Tezepelumab reduces and eliminates OCS use in OCS-dependent patients with severe asthma: Primary results from the phase 3b WAYFINDER study

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Introduction: Tezepelumab is a human monoclonal antibody that blocks thymic stromal lymphopoietin (TSLP) activity. In the phase 3b WAYFINDER study (NCT05274815), the ability of tezepelumab to reduce or discontinue oral corticosteroid (OCS) use without loss of asthma control was investigated over 52 weeks in a larger cohort of OCS-dependent patients with severe asthma.

Methods: WAYFINDER was an open-label, single-arm, OCS-sparing study in adults with severe asthma receiving OCS (prednisone/prednisolone 5-40 mg/day or equivalent) for ≥3 months before study entry. Participants received tezepelumab 210 mg subcutaneously every 4 weeks for up to 52 weeks. After a 4-week induction phase on a stable OCS dose, participants entered a 48-week OCS reduction and maintenance phase. Co-primary endpoints, assessed at weeks 28 and 52, were proportion of participants who reduced their daily prescribed mOCS dose to ≤5 mg/day without loss of asthma control; and proportion of participants who discontinued OCS without loss of asthma control. OCS dose reductions to <5 mg/day were contingent on participants retaining adrenal function, assessed via an initial morning cortisol test and then either adrenocorticotropic hormone stimulation tests or repeated morning serum cortisol tests.

Results: Overall, 273 patients completed the study. The mean (SD) baseline mOCS dose was 10.8 (6.5) mg/day. The proportion of participants who had an mOCS dose of ≤5 mg/day was 88.9% at week 28 and 89.9% at week 52. The proportion of participants who discontinued OCS was 32.2% at week 28 and 50.3% at week 52. 82.2% of participants had an mOCS dose of ≤5 mg/day without loss of asthma control at week 52 when the reason for systemic corticosteroid treatment was related to adrenal insufficiency.

Conclusions: Most patients in this broad severe asthma population treated with tezepelumab achieved clinically meaningful reductions in mOCS dose to ≤5 mg/day or completely discontinued OCS, while maintaining asthma control.

Funding: AstraZeneca and Amgen Inc.

F28

Improvements in asthma exacerbations, lung function, asthma control and health-related quality of life after tezepelumab initiation in patients with severe asthma: Interim results from the US phase 4 PASSAGE study

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Introduction: Clinical trials for severe asthma often exclude or underrepresent key patient populations. The PASSAGE study (NCT05329194) aims to assess tezepelumab effectiveness and safety in a diverse, real-world population of patients with severe asthma in the USA.

Methods: PASSAGE is a 52-week, ongoing, phase 4, multicenter, single-arm, open-label study of patients (≥12 years) with severe asthma. The study includes patients with asthma phenotypes defined by blood eosinophil counts (BECs; ≥/<300 cells/µL) and allergy status (with or without any perennial aeroallergen sensitization) at baseline, and four underrepresented populations: Black/African American patients, adolescents (12–17 years old), patients with comorbid mild to moderate COPD and smokers (≥10 pack-years). Participants are receiving tezepelumab 210 mg subcutaneously every 4 weeks (last dose at week 48). This interim analysis assessed annualized asthma exacerbation rates (AAERs) in the 12-month baseline and treatment periods, and pre-bronchodilator forced expiratory volume in 1 second (pre-BD FEV_1), Asthma Control Questionnaire-6 (ACQ-6), Asthma Impairment and Risk Questionnaire (AIRQ) and St George's Respiratory Questionnaire (SGRQ) scores at baseline, weeks 24 and 52.

Results: Of 208 participants, 41% had BECs ≥300 cells/µL, 56% had confirmed allergy, 17% were Black/African American, 5% were adolescents, 13% had comorbid COPD and 23% were smokers. Overall, AAER decreased by 76% (95% CI: 69, 81); comparable reductions were observed across asthma phenotypes and underrepresented populations. The least-squares mean change from baseline in pre-BD FEV_1 was 0.11 L (95% CI: 0.06, 0.17) at week 24 and 0.15 L (95% CI: 0.10, 0.21) at week 52. Clinically meaningful improvements from baseline were observed in ACQ-6, AIRQ and SGRQ scores at weeks 24 and 52.

Conclusions: This interim analysis of patients with severe asthma treated with tezepelumab provides evidence of reductions in AAERs across asthma phenotypes and underrepresented populations, with improvements in lung function, asthma control and health-related quality of life.

Funding: **AstraZeneca and Amgen Inc.**

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Long-Term Safety and Disease Control of Ruxolitinib Cream in Children Aged 2 to 6 and 7 to 11 Years With Atopic Dermatitis: Results From the TRuE-AD3 Study

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Introduction: Ruxolitinib cream demonstrated efficacy and safety at Week 8 in children aged 2–11 years with mild-to-moderate atopic dermatitis (AD) in TRuE-AD3 (NCT04921969), with similar results among children aged 2–6 and 7–11 years. Here, we report long-term safety and disease control by age subgroup.

Methods: Patients aged 2–11 years with AD, an Investigator's Global Assessment (IGA) score of 2/3, and 3%–20% affected body surface area (BSA) were randomized (2:2:1) to twice-daily ruxolitinib cream (0.75%/1.5%) or vehicle for 8 weeks (no anatomic restrictions) and then remained on ruxolitinib cream or were rerandomized to either ruxolitinib cream regimen for 44 weeks of as-needed treatment. Disease control was assessed by achievement of IGA 0/1 and percentage affected BSA. Safety/tolerability was also assessed.

Results: Of 330 randomized patients, 282 (2–6 years, 49.3%; 7–11 years, 50.7%) were evaluated in the long-term period. Ruxolitinib cream was well tolerated, with no serious treatment-related adverse events during the 52-week study. Among patients initially randomized to ruxolitinib cream, disease control was maintained or further improved in the long-term period in patients aged 2–6 and 7–11 years as assessed by IGA 0/1 (Week 52: 0.75% ruxolitinib cream, 82.9% and 76.7%, respectively; 1.5% ruxolitinib cream, 72.1% and 72.5%) and mean affected BSA (Week 52: 0.75% ruxolitinib cream, 1.8% and 2.2%; 1.5% ruxolitinib cream, 1.8% and 2.0%). Patients who crossed over from vehicle experienced similar levels of disease control.

Conclusions: Ruxolitinib cream demonstrated long-term tolerability and disease control regardless of age group in children with mild-to-moderate AD.

Funding: Incyte Corporation

F30

Patient Preferences for Attributes of Prophylactic Treatment in Hereditary Angioedema: A Discrete-Choice Experiment

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Introduction: Hereditary angioedema (HAE) is a genetic condition that causes recurrent episodes of swelling. New preventative therapies are being researched and approved for HAE, but patient preferences regarding the attributes of these treatments are not well understood.

Methods: Patients were invited to participate in an online survey with a discrete-choice experiment asking respondents to select their preferred preventative treatment from a set of 2 hypothetical alternatives. Each preventative treatment was described in terms of onset of drug action, reduction in attack frequency, mode and frequency of administration, and risks of mild-to-moderate injection site reactions (ISRs) and gastrointestinal (GI) side effects. Choices were modelled using random-parameters logit models to estimate preference weights and calculate the relative importance of attributes and their willingness to accept risks in exchange for improvements in efficacy.

Results: 250 patients, recruited through an HAE patient advocacy group, completed the survey (female, 204 [81.6%]; mean age, 39 years; mean Angioedema Control Test score, 9.7). Overall, patients placed the greatest importance on reduction in attack frequency, treatments taken as an oral tablet as opposed to injections, treatments taken once every 8 weeks as opposed to more frequently, and those with the lowest risk of side effects. Compared with other attributes, relatively less importance was placed on reducing the onset of action. For a large (40%) reduction in attack frequency, patients would accept >50% risk of an ISR and >25% risk of a GI side effect. For smaller (5%) reductions in attack frequency, patients would accept a 19.3% risk of an ISR and a 7.6% risk of a GI side effect.

Conclusions: These results provide insights into the treatment attributes that are most important to HAE patients choosing a long-term preventative treatment. Better understanding patients' preferences for and willingness to trade off treatment attributes may help facilitate shared decision-making.

Funding: **Ionis.**

F31

Pooled REMIX-1/-2 Phase 3 Data: Early and Sustained Symptom Improvement With Remibrutinib in Chronic Spontaneous Urticaria

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Introduction: Remibrutinib, an oral, highly selective Bruton's tyrosine kinase inhibitor, has shown superior efficacy vs placebo in symptom improvement in patients with chronic spontaneous urticaria (CSU).

Methods: REMIX-1/-2 are multicenter, randomized, double-blind, placebo-controlled phase 3 studies assessing the efficacy and safety of remibrutinib in patients with CSU inadequately controlled by second-generation H1-antihistamines. Patients were randomized 2:1 to remibrutinib 25 mg twice daily (BID) or placebo (24 weeks), then continued on open-label remibrutinib 25 mg BID (28 weeks). Mean (± standard deviation [SD]) change from baseline (CFB) (observed data) in weekly Urticaria Activity Score (UAS7), Itch Severity Score (ISS7), and Hives Severity Score (HSS7) of pooled data are presented from Week 1 to Week 52.

Results: The pooled analysis included 606 and 306 patients in the remibrutinib and placebo groups, respectively, who received at least one dose from REMIX-1 and REMIX-2. Remibrutinib showed improvements vs placebo in mean ± SD CFB-UAS7 at Week 1 (−11.8±9.9 vs −3.6±7.6) and Week 24 (−22.4±11.9 vs −15.4±13.3). Improvements were shown for mean CFB-ISS7 at Week 1 (−5.3±4.7 vs −1.8±3.6) and Week 24 (−10.5±5.8 vs −7.4±6.4), and for mean CFB-HSS7 at Week 1 (−6.4±5.7 vs −1.8±4.3) and Week 24 (−11.9±6.8 vs −8.0±7.5). Patients receiving remibrutinib from initiation, and who transitioned to remibrutinib from placebo at Week 24, showed similar improvements at Week 52 (UAS7: −23.1±12.1 and −22.7±11.9; ISS7 −10.9±5.9 and −10.7±6.0; HSS7: −12.2±6.9 and −12.0±6.7). Exposure-adjusted incidence rates of adverse events (AEs), serious AEs, and AEs leading to treatment discontinuation did not increase with treatment up to Week 52.

Conclusions: In REMIX-1/-2, improvements in symptoms with remibrutinib were observed from Week 1 and sustained to Week 52, with a favorable safety profile, suggesting remibrutinib has potential as a novel oral treatment option for fast and sustained symptom relief for patients with CSU.

Funding: Novartis Pharma AG, Basel, Switzerland

F32

No Clinically Meaningful Impact of Remibrutinib on Immunoglobulin Levels Or Infections In Chronic Spontaneous Urticaria

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Introduction: Remibrutinib is an oral, highly selective Bruton's tyrosine kinase (BTK) inhibitor. As BTK plays an important role in immune responses, we analyzed the impact of remibrutinib on total immunoglobulin levels and infection rates in patients with chronic spontaneous urticaria (CSU) in the phase 3 REMIX studies.

Methods: REMIX-1/-2 are multicenter, randomized, double-blind, placebo-controlled studies assessing efficacy/safety of remibrutinib in patients with CSU inadequately controlled by H_1-antihistamines. Patients were randomized 2:1 to remibrutinib 25 mg twice daily or placebo (24 weeks), followed by open-label remibrutinib (28 weeks). We present a pooled data analysis for serum immunoglobulin levels (IgA, IgE, IgG, IgM) assessed at baseline, Weeks 12, 24, and 52, and exposure-adjusted occurrence rate (EAOR) of infection treatment-emergent adverse events (TEAEs) per 100 patient-years.

Results: The safety analysis included 606 and 306 patients in the remibrutinib and placebo groups, respectively. Mean total immunoglobulin levels remained similar over time and between arms. For remibrutinib, mean immunoglobulin levels at baseline and Week 52, respectively, were: IgA, 2.2 g/L and 2.3 g/L; IgE, 528.0 µg/L and 535.0 µg/L; IgG, 11.3 g/L and 10.9 g/L; IgM, 1.1 g/L and 0.8 g/L. Up to Week 24, ≥1 infection-related TEAE occurred in 33.5% (remibrutinib) and 34.3% (placebo) of patients. The EAOR of infection-related TEAEs was 111.7 (remibrutinib) versus 114.7 (placebo) through Week 24, and 89.5 (remibrutinib) through Week 52.

Conclusions: Remibrutinib did not have a clinically meaningful impact on mean total immunoglobulin levels over time. Infection rates were comparable between remibrutinib and placebo and did not increase with long-term treatment.

Funding: Novartis Pharma AG, Basel, Switzerland

F33

Dupilumab Safety and Efficacy in a Real – World Clinical Setting: The RAPID Asthma Registry

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Introduction: Dupilumab, blocks interleukins 4 and 13, key and central drivers of type 2 inflammation, has shown efficacy for the treatment of moderate-to-severe asthma in several clinical trials, but sparse real-world data. RAPID (NCT04287621), a global, prospective registry, characterized patients with asthma initiating dupilumab in real-world clinical practice. This analysis assessed clinical effectiveness and safety of dupilumab.

Methods: RAPID enrolled patients (aged ≥12 years) initiating dupilumab for asthma according to country-specific prescribing information. This analysis included the first 205 patients who completed a full year of the study and assessed unadjusted annualized severe exacerbation rates, asthma control (6-item Asthma Control Questionnaire [ACQ-6] score), quality of life (Asthma Quality of Life [AQLQ] score), and safety. Data shown as mean (SD) unless stated otherwise.

Results: Patients were 50.1 (17.4) years of age, 134 (65.4%) patients were female, 152 (74.1%) of patients were White, and 27 (13.2%) were Black or African American. Patients experienced an average of 1.9 (4.16) severe exacerbations in the year prior to screening. After 1 year of the study, patients (n=205) had an unadjusted annualized severe exacerbation rate of 0.14 Patients (n=195) also had uncontrolled asthma at baseline with an ACQ-6 score of 2.34 (1.93); at Week 52, 51.7% of patients were classed as ACQ-6 responders, with a reduction in baseline ACQ-6 score of ≥0.5. Similarly, patients reported improved quality of life after 52 weeks of the study (AQLQ at baseline: 4.08 [1.32]; change from baseline at Week 52: 1.43 [1.36]). Treatment-emergent adverse events were reported by 99 (48.3%) patients, with asthma (11.7%), COVID-19 (5.9%) and acute sinusitis (4.9%) reported most often.

Conclusions: Patients completing the first year of RAPID had reduced exacerbation rates, improved asthma control and quality of life. Overall safety was consistent with the known dupilumab safety profile.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F34

Clinical Remission and Off-treatment Remission in Pediatric Patients with Moderate-to-Severe Atopic Dermatitis Treated with Dupilumab: Preliminary Data from an Open-label Extension Study

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Introduction /Objective: Higher severity and earlier disease onset are predictive factors for atopic dermatitis (AD). Despite dupilumab's approval in young AD patients starting from 6 months age, lifelong treatment is a common concern among prescribers and caregivers This interim analysis reported paediatric patients on dupilumab achieved clear or almost clear skin during treatment and maintained clear, almost clear, or mild AD after treatment cessation.

Materials and Methods: The analysis included 6 months to 17 years old moderate-to-severe AD patients (N=738; 6 months - 5 years: 163; 6 -11 years: 327; 12 -17 years: 248) enrolled in double-blind, randomized, placebo-controlled clinical trials continuing ongoing LIBERTY AD PED open-label extension study (NCT02612454). Clinical remission achieved with clear or almost clear skin (Investigator's Global Assessment (IGA) score of 0/1) for at least 12 weeks (3 consecutive monthly visits) after 40 weeks on dupilumab. Patients reaching clinical remission discontinued dupilumab with monthly monitoring to assess time on remission off treatment. Patients with mild, moderate or severe AD (IGA score ≥2 at any one visit), re-started treatment. Interim analysis identifies patients across all age groups achieving clinical remission within 18 month (1.5 years) follow up period.

Results: About one third of pediatric patients (N = 276/738, 37.4%; 6 months-5years: 54/163, 33.1%; 6-11years: 122/327, 37.3%; 12-17years: 100/248, 40.3%) achieved clinical remission81.9% infants and preschoolers, 79.7% children, and 75.0% adolescents who experienced clinical remission had clear, almost clear, or mild AD (IGA 0/1 or 2) at 52 weeks from first clinical remission.

Conclusion: One third of study population ages 6 months to 17 years with moderate-to-severe AD on dupilumab experienced clinical remission. Of these majority had clear, almost clear, or mild AD at 52 weeks from first clinical remission. Younger patient populations had higher probability of maintaining minimal or no disease activity after dupilumab treatment cessation.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F35

Treatment with Navenibart (STAR-0215) Reduces Attack Severity and Use of Rescue Medication in Patients with Hereditary Angioedema (HAE): Interim Results from the ALPHA-STAR Trial

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Introduction: Interim data were reported from an ongoing Phase 1b/2 clinical trial (ALPHA-STAR, NCT05695248), demonstrating a favorable safety profile with reductions in HAE attack frequency.

Methods: Adults with HAE-C1INH Type 1 or Type 2 were recruited into 3 dose cohorts. Cohort 1: 450 mg (day 1); Cohort 2: 600/300 mg (day 1/84); Cohort 3: 600 mg (day 1/28), all treated by navenibart subcutaneous injection. HAE attack severity (mild/moderate/severe) and the number of HAE attacks requiring on-demand therapy from participants who completed a 3- or 6-month follow-up (interim data cut-off 13-Mar-2024) are reported.

Results: The mean age (SD) of study participants (n=16) was 46 (20) years; 56% were female. After initiation of treatment with navenibart, at 3-month follow-up (data for 14/16 participants available at cut-off), baseline monthly rates (mean) of mild/moderate/severe HAE attacks/month of 0.95/1.25/0.11 were reduced to 0.13/0.05/0.00; at 6-month follow-up (data from 7/16 participants available at cut-off), baseline monthly rates (mean) of mild/moderate/severe HAE attacks/month of 0.45/1.54/0.14 were reduced to 0.10/0.08/0.00. For the same participants at 3-/6-month follow-up, rates (mean) of HAE attacks/month requiring rescue medication were reduced from 1.86/1.32 at baseline to 0.16/0.10 post-treatment with navenibart. No serious treatment emergent adverse events or treatment discontinuations were reported.

Conclusions: This interim analysis suggests that navenibart reduces the burden of HAE, assessed by reduction in HAE attack frequency, severity, and use of rescue medication. No safety issues were identified.

Funding: Astria Therapeutics, Inc.

F36

Dupilumab Efficacy in Patients with Chronic Obstructive Pulmonary Disease (COPD) with Type 2 Inflammation across Baseline Eosinophil Counts

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Introduction: Type 2 (T2) inflammation in patients with chronic obstructive pulmonary disease (COPD) is evidenced by elevated blood eosinophil counts (BEC), often correlating with higher risk for exacerbations. The *post-hoc* analysis of pooled data from BOREAS and NOTUS evaluated efficacy of dupilumab in patients stratified by baseline BEC of ≥150 cells/µL/≥300 cells/µL.

Methods: BOREAS (NCT03930732) and NOTUS (NCT04456673), both phase 3, randomized, placebo-controlled trials, enrolled 1,874 patients with COPD, moderate-to-severe airflow limitation, and T2 inflammation. Patients were randomized to dupilumab 300 mg or placebo q2w for 52 weeks. This analysis included patients from the intention-to-treat (ITT) population of BOREAS and NOTUS, stratified by baseline BEC≥150 cells/µL, 150-300 cells/µL or ≥300 cells/µL. Endpoints included annualized moderate-to-severe exacerbation rate, change from baseline to Week 52 in pre- and post-bronchodilator forced expiratory volume in 1 second (FEV_1) and St. George's Respiratory Questionnaire (SGRQ) total score.

Results: Of 1,873 patients, 1,703 (dupilumab n=855; placebo n=848) had baseline BEC≥150 cells/µL, and 1,135 (dupilumab n=573; placebo n=562) had baseline BEC≥300 cells/µL. Dupilumab vs placebo reduced annualized exacerbation rates by up to 36.9%. At Week 52, dupilumab vs placebo improved pre-bronchodilator FEV_1 by (LS mean difference [95%CI]) 0.07 (0.04,0.11)L in the ITT population, 0.08 (0.04,0.11)L in patients with baseline BEC≥150 cells/µL, and 0.09 (0.05,0.13)L with baseline BEC ≥300 cells/µL. Similar results were observed for changes in post-bronchodilator FEV_1. Dupilumab reduced SGRQ total scores at Week 52 by (LS mean [95%CI]) −3.37 (−4.95,−1.78) (ITT population), −3.07 (−4.7,−1.44) (baseline BEC≥150 cells/µL), and −3.98 (−6.01,−1.95) (baseline BEC≥300 cells/µL). Overall safety of BOREAS and NOTUS was consistent with known dupilumab profile.

Conclusions: In patients with COPD and T2 inflammation, dupilumab reduced annualized exacerbation rates, and improved lung function and quality of life with slightly greater treatment effects observed in patient with higher baseline BEC.

Funding: Sanofi and Regeneron Pharmaceuticals Inc

F37

Health Care Resource Utilization (HCRU) of Patients With Chronic Spontaneous Urticaria (CSU) by Disease Control: Results From a United States (US) Claims Database Study

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Introduction: CSU is characterized by the spontaneous occurrence of itch, wheals, and/or angioedema lasting >6 weeks without a specific identifiable trigger; prevalent in 0.23% to 0.78% of the US population. Uncontrolled CSU has been associated with increased clinical and economic burden. Here, we investigated HCRU in patients with CSU stratified by disease control in the US.

Methods: This real-world analysis utilized data of patients aged ≥18 years with a confirmed diagnosis of CSU between January 2016 and October 2023 from the US HealthVerity health insurance claims database. HCRU according to patients with/without disease control was assessed during the 1 year prior to (baseline period) the date of CSU diagnosis (index date), and all available HCRU following CSU diagnosis (follow-up). Lack of disease control was defined using proxy events: any CSU-related inpatient admission, emergency department (ED) or urgent care visit, or use of systemic corticosteroids, biologics, or immunosuppressants post index date. For the corticosteroid use proxy event, patients were required to have a CSU-related visit, regardless of setting, ≤15 days prior to systemic corticosteroid prescription. Results were summarized using descriptive statistics.

Results: Overall, 224,958 patients were included; 76.3% were female and mean age was 44.3 years. Uncontrolled CSU was experienced by 50.6% of patients. Most patients (56.8%) experienced uncontrolled CSU ≤60 days post index date. All-cause HCRU parameters increased from baseline to follow-up. Additionally, patients with uncontrolled relative to controlled disease had greater CSU-related HCRU: inpatient admissions, 8.1-fold; ED visits, 5.4-fold, and urgent care visits, 3.5-fold; during a follow-up of 2.5 and 2.2 years, respectively (Table 1). Similar outcomes reported for all-cause HCRU (Table 2).

Conclusions: We observed an increase in all-cause HCRU parameters post CSU diagnosis, and in CSU-related HCRU in patients with uncontrolled disease relative to controlled disease, highlighting a need for more effective therapeutic intervention.

Funding: Novartis USA.

F38

Angioedema in Chronic Spontaneous Urticaria (CSU) is Associated with Greater Health Care Resource Utilization (HCRU): Results From a United States (US) Claims Database Study

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Introduction: CSU is a skin condition characterized by the occurrence of itch, wheals, and/or angioedema lasting >6 weeks without an identifiable trigger. In patients with CSU, a history of angioedema has been associated with increased disease severity and duration. Here, we investigated treatments and HCRU in patients with CSU, with/without angioedema, in the US.

Methods: This real-world analysis utilized data of patients aged ≥18 years with a record of CSU diagnosis (January 2016-October 2023) from the US HealthVerity health insurance claims database. Treatments, specialist physician visits, and HCRU were assessed following CSU diagnosis (follow-up) and stratified by the presence/absence of angioedema. This was defined as patients with ≥1 claim vs no claims with an angioedema diagnosis code during the first year of follow-up (including the time of CSU diagnosis [index date]). Results were summarized using descriptive statistics.

Results: Of 224,958 patients with CSU, 19.2% had angioedema and 80.8% did not have angioedema. The mean patient age (index date) in both groups was similar and most were female (with angioedema: 44.5 years, 74.7% female; without angioedema: 44.3 years, 76.7% female). Antihistamines, corticosteroids, and biologics were prescribed more frequently in patients with (58.4%, 73.8%, and 13.3%) relative to without (53.7%, 59.3%, and 9.2%) angioedema, respectively. Allergist/immunologist visits were 1.5-fold higher among patients with (43.0%) relative to without (28.6%) angioedema. A higher proportion of CSU-related inpatient admissions (23.9% and 12.8%), emergency department visits (22.9% and 10.4%), and urgent care visits (8.1% and 5.9%) were reported in patients with relative to without angioedema, respectively (Table).

Conclusions: Among patients with CSU, HCRU was more frequent in those with angioedema relative to those without, despite those with angioedema generally receiving more guideline-recommended treatments. Overall, biologic treatment was limited, and corticosteroid use was frequent. This suggests undertreatment of this patient group and the need for more effective therapeutic options.

Funding: Novartis USA.

F39

Living with HAE with Normal C-1 Inhibitor: The Worry of When

Kristie Cline, MBA; Erin Slattery; Michelle Slattery

Introduction: Hereditary angioedema (HAE) is a rare disease that causes potentially life-threatening angioedema. There are three types of HAE: Type I with low levels of C1-inhibitor plasma protein; Type II with non-functioning C1-inhibitor; and HAE with normal C1-inhibitor, (HAE-nl-C1INH, previously Type III) with normal levels and functioning C1-inhibitor. Patient insights are necessary to understand life treatment preferences and disease impacts on quality of life.

Methods: Two virtual advisory meetings were conducted in November 2024 with 7 women ages 21-60, with HAE-nl-C1INH.

Results: The number one cause of anxiety in participants was the uncertainty of when a swell will occur. Additional sources of anxiety: severity of potential swells; insurance and challenges in maintaining supply of rescue medication; and a perception that doctors don't understand HAE.
Breakthrough swells were reported to be frequent even with prophylactics. Six of the seven participants used prophylactic HAE medication. All used rescue (acute) medications for swells consistent with US HAE Association (HAEA) guidelines. Participants reported using either icatibant or recombinant C1INH rescue medications. Four participants reported treating three or more swells with rescue medication per month. Most reported they would treat more swells if they had an unlimited supply of rescue medication.
Pain during swells was ranked an average of 7.7 out of 10, which was defined as severe-to-intense and activity limiting. Participants reported daily pain.
Participants ranked having a swell totally resolved in one dose, rescue medication that is easy transport on the go, and swells resolved in a specific timeframe as top desired qualities of rescue medication.

Conclusions: Improved resources are needed for communication with healthcare professionals, especially regarding pain and complete swell resolution. Mental health support is needed to manage the anxiety of HAE swells. Additional research is suggested to explore variances in response to prophylactic and/or rescue treatment, swell frequency, severity, and pain among those living with HAE-nl-C1INH.

Funding: Pharming Healthcare, Inc.

F40

Patient Insights Expand Understanding of APDS

Kristie Cline, MBA; Michelle Slattery; Erin Slattery

Introduction: Discovery of primary immunodeficiencies (PIs) has rapidly increased, from 180 known PIs[1] in 2012 to more than 450 today[1]. Patient perspectives are essential to deepen understanding of these conditions and, in turn, improve health outcomes. Patient advisory meetings provided insights into experiences with Activated PI3K Delta Syndrome (APDS), a PI named in 2013[1].

Methods: A virtual advisory board meeting was conducted in 2024 with 7 patients living with APDS.

Results: Participants reported symptoms not commonly reported in published literature including fatigue, brain fog, joint and diffuse pain, temperature sensitivity, headaches, and dental issues. Apart from headache and dental issues, these symptoms were also reported in a 2023 patient advisory meeting by a separate cohort of 7 people living with APDS.

Participants' disease understanding was limited, with low awareness of common symptoms and signs of APDS, including autoimmune or autoinflammatory conditions, frequent and severe diarrhea, and developmental and cognitive delays.

Participants expressed challenges with physicians understanding of APDS, believing their symptoms, and coordination of care. For example, 5 of 7 participants experienced diarrhea which was misdiagnosed or overlooked in all but one. Participants had up to nine physicians for their APDS-related conditions and take many medications.

Fatigue, brain fog, and pain impact quality of life. All participants experienced frequent fatigue, daily for more than half. Brain fog impacts most participants a few times each week, and many live with daily pain. Three participants were unable to work.

Conclusions: More patient-friendly APDS education resources are needed. Additional research is suggested to confirm the prevalence of previously unreported symptoms in those living with APDS. Research is also suggested to explore challenges in disease understanding specifically analyzing the impacts of brain fog, developmental delays, socioeconomic impacts, or potential variance in the expression of APDS based on genetic variants.

Funding: Pharming Healthcare, Inc.

F41

ARS-1 (epinephrine nasal spray) development, from pharmacokinetics and pharmacodynamics to real-world data in pediatric food allergy patients

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Introduction: No clinical trials were conducted to support pediatric doses of epinephrine injection products for the treatment of severe allergic reactions. Instead, FDA approval was based on epinephrine's well-established safety and efficacy. During the development of ARS-1, a pharmacokinetic/pharmacodynamic study and an oral food challenge (OFC) study in pediatric patients were conducted.

Methods: The pharmacokinetic/pharmacodynamic study was a Phase 1, single-dose, open label study with allergy patients aged 4 to 17 (N=42). The OFC study was a Phase 3 study in food allergy patients aged 6 to 17 who received ARS-1 following onset of moderate anaphylaxis symptoms (N=15). In both studies, patients received ARS-1 1 mg (15-30 kg) or 2 mg (≥30 kg).

Results: Mean epinephrine concentration-time profiles were similar between 1 and 2 mg (C_{max} of 690 and 651 pg/mL, respectively). Median time to resolve moderate anaphylaxis symptoms was 16 minutes, with no patient requiring a second dose of ARS-1. One patient developed a biphasic reaction 2 hours and 45 minutes following ARS-1 administration and received intramuscular epinephrine. Pharmacodynamic data from these studies were similar, except for a more pronounced decrease in diastolic blood pressure at early time points in younger patients in the OFC study. Adverse events were mild/moderate and resolved quickly.

Conclusion: ARS-1 is the first epinephrine nasal product studied in pediatric patients. Pharmacodynamic data were consistent between studies, and the OFC study demonstrated that ARS-1 can resolve anaphylaxis symptoms. ARS-1 is expected to be a safe and effective needle-free treatment option for pediatric allergy patients.

Funding: ARS Pharmaceuticals

F42

Use of Intranasal Epinephrine (Neffy) in a Patient Who Experienced Anaphylaxis to Subcutaneous Allergen Immunotherapy

Hary T. Katz, M.D.

Introduction: Epinephrine is the only approved first-line treatment for severe allergic reactions, including anaphylaxis. Until recently, epinephrine administration was limited to parenteral formulations. However, the August 2024 FDA approval of intranasal epinephrine (neffy) has provided patients with a needle-free option that is anticipated to reduce dosing hesitancy. Extensive pharmacokinetic (PK) and pharmacodynamic (PD) data have demonstrated that neffy has PK and PD profiles that are comparable to or better than parenteral formulations. However, ethical and practical limitations preclude large-scale efficacy studies in anaphylactic patients, potentially leading to prescribing reluctance. We report a case where neffy was successfully used in a patient experiencing a systemic allergic reaction following subcutaneous immunotherapy (SCIT).

Case Presentation: A 10-year-old female with a history of allergic rhinitis, atopic dermatitis, and shellfish allergy developed diffuse pruritus and persistent coughing approximately 45 minutes following inhalant allergen SCIT. On exam, she appeared anxious, was repeatedly coughing, and had flushing involving her face, neck and anterior chest. She had expiratory wheezes bilaterally. Her heart rate was elevated at 96 bpm, with respiratory rate, blood pressure and oxygen saturation within normal limits. She was administered neffy 2 mg, cetirizine 10 mg PO, and nebulized albuterol 2.5 mg. Significant improvement in all symptoms was observed within 5 minutes. No further treatment was required, and she was observed for 60 minutes with complete resolution of symptoms.

Conclusion: A paucity of data regarding neffy's clinical effectiveness may lead to prescribing reluctance. The present case demonstrates the use of neffy to successfully treat anaphylaxis in a pediatric patient following SCIT. This case report is part of a growing body of evidence, demonstrating real-world efficacy and should alleviate concern among providers to prescribe this agent.

Funding: ARS Pharma

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F43

Pharmacokinetics by Epinephrine Products from Various Studies

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Introduction: Despite its long history of clinical use, there is limited pharmacokinetic (PK) data on acute doses of epinephrine, particularly regarding how PK is influenced by the route of administration. Recent comparative PK studies have highlighted significant differences among delivery methods, emphasizing the need for further investigation.

Methods: During the development of an intranasal (IN) epinephrine spray for the treatment of severe allergic reactions, multiple PK studies were conducted, each with sample sizes generally exceeding 30 subjects. This analysis included nine studies evaluating epinephrine administration via:

- **IN epinephrine spray 2 mg** (n=13, 42, 36, 42, 42)
- **Manual intramuscular (IM) injection (0.3 mg, 21/22G x 1")** (n=67, 36, 42, 31, 42)
- **Cartridge-based epinephrine autoinjector (AAI) 0.3 mg** (n=35, 13, 42)
- **Syringe-based AAI** (n=13, 36)

Mean plasma epinephrine concentrations over time were assessed and compared across administration routes.

Results: PK profiles demonstrated comparability among IN epinephrine spray 2 mg, IM 0.3 mg, and syringe-based AAIs, while cartridge-based AAIs exhibited greater PK variability. The maximum concentration (Cmax) ranges were:

- **IN epinephrine spray 2 mg:** 421–570 pg/mL
- **IM 0.3 mg:** 232–339 pg/mL
- **Syringe-based AAI:** 359–363 pg/mL
- **Cartridge-based AAI:** 311–714 pg/mL

Conclusion: IN epinephrine spray, IM injection, and syringe-based AAIs provided consistent PK profiles, whereas cartridge-based AAIs showed higher variability, likely due to greater injection force. These findings suggest that IN epinephrine may serve as a viable, needle-free alternative to IM administration for severe allergic reactions, offering comparable PK performance with potential advantages in ease of use and patient preference.

Funding: ARS Pharmaceuticals, Inc

F44

Clinical Predictors of Asthma Remission: A Post Hoc Analysis of the ATLANTIS Study

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Introduction: The assessment of small airways involvement in asthma (ATLANTIS[1]) study was conducted to identify biomarkers and physiologic testing parameters associated with small airways dysfunction in asthma. Remission of asthma is an emerging paradigm of disease management, recently recognized as a management objective by several international guidelines.[2,3] However, baseline predictors of remission need to be further clarified. This analysis aimed to assess predictors of asthma remission in a cohort of patients in the ATLANTIS study.

Methods: A retrospective, exploratory analysis was conducted. Remission was defined as: Asthma Control Questionnaire-6 (ACQ-6) < 1.5, no maintenance oral corticosteroids (OCS), no exacerbations and a pre-bronchodilator FEV_1 % predicted absolute decline < 10% over 12 months of follow-up. Multivariate logistic regression assessed potential predictors of remission.

Results: Asthma remission was achieved in 45.2% of patients. Predictors of remission included low fractional exhaled nitric oxide (FeNO) (OR: 2.06, 95%CI: 1.05 - 2.53), male gender (OR: 2.06, 95% CI: 1.40-3.20), and low post bronchodilator FEV_1 % predicted (OR: 1.02, 95% CI: 1.01-1.04). Risk factors for not achieving remission included prior exacerbation history (OR: 0.405, 95% CI: 0.226-0.726), presence of severe asthma (OR: 0.570, 95% CI: 0.333-0.975) and high BMI (OR: 0.960, 95% CI: 0.926-1.00). Fewer GINA 4-5 asthma patients achieved remission (31.7% vs. 58.8% not in remission, $p < 0.001$). More patients with high T2 biomarkers failed to achieve remission (12.1% vs. 6.92%, $p = 0.01$).

Conclusions: This post-hoc analysis demonstrated clear differences between patients who achieved remission versus those who did not. The study showed several predictors of asthma remission including FeNO, male gender, and low post bronchodilator FEV_1 % predicted.

Funding: **Chiesi Farmaceutici S.p.A.**

F45

Stringent efficacy response of skin clearance and itch-free state with abrocitinib 100 mg versus dupilumab in patients with moderate-to-severe atopic dermatitis: a post hoc analysis of JADE COMPARE

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Introduction: Patients with treatment-refractory atopic dermatitis (AD) may require systemic therapies to gain disease control, including dupilumab, an injectable interleukin-4 receptor alpha antagonist, and abrocitinib, a once-daily, oral, Janus kinase 1-selective inhibitor. In phase 3 JADE DARE (NCT04345367), more patients achieved ≥90%/100% improvement from baseline in Eczema Area and Severity Index (EASI-90/-100) with abrocitinib 200 mg versus dupilumab 300 mg, with concomitant topical medicated therapy, from Weeks 2–26. Further, more patients achieved EASI-90 (i.e., near complete/complete skin clearance) plus Peak Pruritus Numerical Rating Scale score of 0 or 1 (PP-NRS 0/1; i.e., itch-free state) with abrocitinib versus dupilumab from Weeks 2–26. Here, we evaluated the efficacy of abrocitinib 100 mg versus dupilumab or placebo in achieving stringent outcomes in phase 3 JADE COMPARE (NCT03720470).

Methods: Data were included from adults who received abrocitinib 100 mg, dupilumab 300 mg (following a 600-mg loading dose), or placebo with concomitant topical medicated therapy in JADE COMPARE. The proportions of patients achieving EASI-90+PP-NRS 0/1, EASI-100, and Investigator's Global Assessment score of 0 (IGA 0) were assessed to Week 16.

Results: Data were analyzed from 238, 242, and 131 patients treated with abrocitinib 100 mg, dupilumab, and placebo, respectively. As early as Week 2, a greater proportion of patients achieved EASI-90+PP-NRS 0/1 with abrocitinib 100 mg versus dupilumab and placebo and continued to increase through Week 16 (20.2% vs 15.5% and 5.4%). Similarly, at Week 16, more patients treated with abrocitinib 100 mg versus dupilumab and placebo achieved EASI-100 (12.7% vs 5.2% and 4.0%) and IGA 0 (12.6% vs 6.5% and 4.8%).

Conclusions: More patients treated with abrocitinib 100 mg achieved near complete/complete skin clearance plus an itch-free state than with dupilumab or placebo. Abrocitinib 100 mg may provide a complete and robust response in patients with moderate-to-severe AD.

Funding: Pfizer Inc.

F46

Systemic JAK1 inhibition by abrocitinib in patients with moderate-to-severe atopic dermatitis is associated with decreased lesional skin *Staphylococcus aureus* abundance and increased microbial diversity

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Introduction: Atopic dermatitis (AD) is characterized by alterations in the skin microbiome, notably increased *Staphylococcus aureus* (*S. aureus*) colonization and decreased microbial diversity compared with healthy skin. Treatment with dupilumab, an injectable interleukin-4 receptor alpha subunit antagonist, is associated with decreased *S. aureus* colonization and increased microbial diversity in AD skin. The effect of the Janus kinase 1 (JAK1)-selective inhibitor abrocitinib on the AD skin microbiome and associations with clinical improvement remain uncharacterized. This post hoc analysis of the phase 2a trial JADE MOA (NCT03915496) aimed to evaluate the effect of abrocitinib on skin microbial diversity and *S. aureus* abundance in in patients with moderate-to-severe AD, and to investigate whether changes in the skin microbiome correlated with clinical improvements.

Methods: Data were included from patients with moderate-to-severe AD treated with once-daily abrocitinib (200 mg, n=14; 100 mg, n=15) or placebo (n=14) for 12 weeks. Skin microbiota were analyzed using 16S rRNA gene sequencing from swabs collected from lesional and nonlesional skin at baseline and Weeks 2 (lesional only), 4, and 12.

Results: Significant differential clustering of treatment groups was observed by Week 2 in lesional skin and Week 4 in nonlesional skin using Bray-Curtis dissimilarity ($P<0.05$). At Week 12, *Staphylococcus* and *S. aureus* abundance were significantly reduced with abrocitinib 200 mg in lesional skin versus baseline and placebo (false discovery rate <0.05). In lesional and nonlesional skin, abrocitinib 200 mg significantly increased microbial alpha diversity (Inverse Simpson index) at Week 12 ($P<0.05$). Decreased *S. aureus* and *Corynebacterium* abundance in lesional skin and increased *Corynebacterium* abundance in nonlesional skin correlated with improvements in clinical metrics with abrocitinib 200 mg treatment ($r>0.5$, $P<0.05$).

Conclusions: These findings link JAK1 inhibition to normalization of cutaneous dysbiosis and clinical improvement, expanding the understanding of mechanisms underlying abrocitinib efficacy in AD.

Funding: Pfizer Inc.

Eastern Allergy Conference
May 29 - June 1, 2025 ~ Palm Beach, FL

Scientific Posters S1-S46 will be on display in the Ponce Foyer during the coffee break, 10:00 – 10:45 am, Saturday May 31, 2025

Not for CME Credit

S1

Going Nuts Over Food Allergies: A Quality Improvement Project

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Introduction: Food allergies are a significant public health concern, with peanut allergy being particularly persistent. The LEAP study demonstrated the efficacy of early peanut introduction in high-risk infants for preventing peanut allergy development. This study aims to improve resident physician education and subsequent parental guidance regarding early food allergen introduction. We hypothesize that targeted resident training will increase the rate of discussion on food allergen introduction during the 6-month well-child visit.

Methods: A quality improvement project was implemented to educate pediatric residents about the importance of early food allergen introduction. The allergens are listed as tree nuts, peanuts, shellfish, eggs, dairy, soy, sesame, fish). This included emails and a dedicated morning conference. A brief, anonymous survey was administered to parents at the 6-month visit to assess whether residents discussed food allergen introduction.

Results: Analysis showed that 86.4% of our pediatric residents discuss food introduction at the 5 months visit, and 77.3% of residents discussed food allergen introduction with parents during the 6-month visit. Parents also reported that 78.2% of residents discussed what an allergic reaction is and 77.2% discussed what an anaphylaxis reaction is.

Conclusion: This initial data suggests that targeted resident education can improve the integration of food allergen introduction counseling into routine well-child visits. Our residents are doing an appropriate job at educating parents but not meeting our goal of 90%. Further analysis and ongoing quality improvement initiatives are necessary to optimize resident training and ensure consistent, high-quality patient care.

S2

Video Procedural Training Series as a means of Onboarding to an Allergy Entrustable Professional Activity (EPA)

Eshika Kohli, BS, Kirandeep Sehmi, MD, Christine Kurien, DO, Henry Blunk, DO, Kate McDonough, Shan Shan Wu, DO, Robert W. Hostoffer, Jr., DO

Introduction: Preparatory materials for an entrustable professional activity (EPA) have been suggested in both Undergraduate Medical Education (UME), Graduate Medical Education (GME), and fellowship training for various specialties. Materials to prepare incoming fellows for their allergy EPA during their allergy/immunology fellowship are limited across the United States. In-person procedural education has been the standard to teach incoming fellows about EPA. We found that an introductory film to the specific allergy EPA prepared the fellows for their new procedural challenges.

Methods: Three videos were developed for onboarding based on common EPA (skin testing, PFT/FENO, and patch testing) utilized in the field of allergy/immunology. A survey was developed for the videos based on a 5-point Likert scale. Pre- and post-surveys were administered to incoming and prior cohort fellows to assess their procedural competency through self-assessment. Microsoft Excel was used to conduct one-tailed t-tests of each video and create visuals to depict the findings.

Results: The data suggests that the videos increased the new fellows' understanding and self-assessed competency of EPAs. Likert scale data was analyzed via a parametric analysis using a one-tailed t-test that yielded significant findings for all three videos (PFT/FENO p= 0.000006, scratch p= 0.000001, patch p=0.000149). The analysis also demonstrated average increase of 42% for PFT/FENO testing, an average increase of 32.12% for scratch testing, and an average increase of 40% for patch testing.

Conclusion: There is a lack of procedural education materials for onboarding application of allergy EPAs for incoming allergy/immunology fellows. Past fellows have primarily been taught through in-person training without orientation. We have developed three videos to streamline procedural training of EPAs for allergy/immunology fellows. This study showcases how a video procedure can be an effective modality to strengthen EPAs.

S3

From Sweet to Swollen: The Unexpected Link Between Soursop and ACE Inhibition Leading to Acute Angioedema

Amber Chen, MD, MBA, Ashley T. Nguyen, MD, Nicholas Gregory, MD, Russell Settipane, MD

Introduction: Soursop or graviola fruit (*Annona muricata*) is a member of the tropical fruit-bearing Annonaceae family. Certain members of this family have angiotensin-converting enzyme (ACE) inhibition activity.[1] This investigation details a case of acute angioedema after consumption of soursop.

Case Description: A 46-year-old woman with no past medical history presented after an acute episode of now pruritic angioedema of her face, lips, and hand without urticaria which occurred following consumption of four to five glasses of homemade soursop beverages. Symptoms lasted five days and required an emergency room visit, where she received intravenous steroids. She denies any previous similar episodes and no other triggers identified. She reported taking one dose of nifedipine around symptom onset. Her symptoms resolved and have not recurred over the next 5 months. She has avoided soursop since the episode. Given the temporal relationship between soursop consumption and symptom onset along with lack of other identifiable triggers, a probable diagnosis of acute angioedema secondary to soursop ingestion was made.

Discussion: Acute angioedema is a rare but potentially life-threatening condition characterized by rapid swelling of skin and mucous membranes, typically affecting face, tongue, lips, and airway. One mechanism involves dysregulation of the bradykinin pathway. Increased bradykinin may cause fluid leakage from blood vessels resulting in swelling. A key regulator of this pathway is ACE, which breaks down excess bradykinin. Angioedema caused by ACE inhibitors is well-documented. However, angioedema caused by soursop is not well studied. Evidence suggests that soursop may contain bioactive compounds that inhibit ACE. This case highlights the potential for soursop to cause ACE inhibition and thus angioedema. This information may help identify angioedema triggers for unexplained episodes in patients with risk factors and from diverse backgrounds. Furthermore, this highlights the need to investigate the mechanisms underlying this phenomenon.
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S4

Safety of Dupixent (Dupilumab) Use During Pregnancy: A Composite Evaluation of Pregnancy Outcomes

Frank Ventura, MD and Steven Clayton, MD

Introduction: Dupilumab (Dupixent) is a monoclonal antibody targeting IL-4 and IL-13 pathways, increasingly used to treat asthma, eczema, and eosinophilic esophagitis (EoE). Currently, there is minimal literature evaluating the safety of Dupixent during pregnancy. This study assesses whether Dupixent use is associated with increased pregnancy complications.

Methods: We conducted a multicenter, retrospective study of pregnant patients exposed to Dupixent compared with age- and comorbidity-matched controls not receiving biologic therapy. The primary outcome was the composite rate of any pregnancy-related complication. Multivariate logistic regression was used to calculate the odds ratios and confidence intervals. Data was analyzed both with no covariates and with four covariates (adjusted for age, race/ethnicity, hypertension, and parity). Patients with pre-existing diabetes mellitus (DM) were excluded from the adjusted analysis due to a zero-cell phenomenon.

Results: Among 11,843 patients with charted Dupixent use, 69 were exposed during pregnancy. Of these, 39 had asthma, 37 had eczema, and 3 had EoE. The duration of Dupixent exposure varied widely, with 29 patients discontinuing during the first trimester, 9 in the second trimester, 5 in the 3rd trimester, and 28 patients continuing throughout pregnancy. The overall complication rate was 66.7% in the Dupixent group vs. 60.9%% in controls (p = 0.5861). The most prominent complications were gestational diabetes, gestational hypertension, pre-eclampsia, unplanned c-sections, and spontaneous abortion. In the adjusted analysis (n = 129), Dupixent exposure was not associated with increased complications (adjusted OR 1.131, 95% CI: 0.505–2.533, p = 0.7650). Findings were consistent across unadjusted and adjusted models.

Conclusion: Dupixent exposure during pregnancy was not associated with an increased risk of pregnancy complications. These findings support the relative safety of Dupixent in pregnancy and provide reassurance to clinicians managing asthma, eczema, or EoE. Larger prospective studies are needed to confirm these results and assess long-term maternal and neonatal outcomes.

S5

Provider perspectives on the iREACH peanut allergy prevention intervention: A qualitative analysis using a rapid framework analysis approach

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Introduction: Peanut allergy (PA) has an estimated prevalence of 2.2% among U.S. children. The LEAP trial demonstrated that early and consistent peanut introduction reduces PA risk by 80%, leading to the "Addendum Guidelines for the Prevention of Peanut Allergy in the United States" (PPA guidelines). iREACH, a set of scalable implementation strategies including education modules, a clinical decision support (CDS) tool, and parent handouts, was developed to support clinician adherence to the PPA guidelines. Results of a cluster randomized controlled trial found iREACH to be effective at increasing pediatric clinician adherence to the PPA guidelines. This study explores provider perspectives on PPA guideline implementation determinants and iREACH implementation strategies, to bridge the gap between clinical evidence and practice.

Methods: We contacted pediatric clinicians (pediatricians and nurse practitioners) in Illinois to participate in key informant interviews. We developed a semi-structured interview guide based on the updated Consolidated Framework for Implementation Research (CFIR) to explore implementation determinants and perspectives on iREACH strategies. Two research coordinators conducted all interviews over Zoom. Rapid analysis using the CFIR framework supported the identification of key themes.

Results: We interviewed 19 clinicians across 12 different practices. Most respondents were female (79%), non-Hispanic White (52.6%), and held medical degree versus nursing degrees (79%). PPA guideline implementation was influenced by information flow into primary care settings, time constraints, leadership support, and clinician motivation, capacity, and culture. Outer setting determinants influencing guideline adherence included parental attitudes and available referral networks. Respondents found a CDS tool helpful for initiating peanut introduction discussions and streamlining test orders and referrals. Education modules were viewed as generally acceptable but sometimes lengthy.

Conclusion: This study illustrates the implementation determinants that may affect guideline adherence and the potential of iREACH implementation strategies to support pediatric clinicians to integrate peanut allergy prevention efforts into their practice.

Funding: NIAID: U01AI138907

S6

Atypical Carcinoid Presenting as Reversible Obstruction with Wheeze

Issac Soto, MD and Nicole Barberis, MD

Introduction: Pulmonary carcinoid tumors belong to a subset of neuroendocrine tumors (NETs). Pulmonary carcinoid tumors are rare and represent an estimated 1-2% of all lung cancers.[5][9] Atypical carcinoid is defined by two to ten mitoses per 10 high-powered fields and evidence of necrosis.[7] Due to the significant overlap of symptoms with respiratory conditions like asthma, COPD, and infection, diagnosis is often delayed.[12] Bronchopulmonary carcinoid tumors often present with non-specific symptoms such as wheezing, recurrent pneumonias, cough, and hemoptysis.[1] Symptom severity often correlates with the tumor size and location. In rare cases, less than 5% of patients may develop carcinoid syndrome.[8] We present the case of a patient with obstructive symptoms, initially presumed to have asthma, whose lack of improvement led to further evaluation and discovery of a bronchopulmonary carcinoid tumor.

Case presentation: A 45-year-old female without significant past medical history was referred for persistent wheezing despite multiple steroid courses and ICS. No features of rhinitis, atopic dermatitis, chronic sinusitis, GERD, or NSAID sensitivity. Normal vitals. Diffuse inspiratory and expiratory wheezing with poor air movement on physical. Spirometry demonstrated an obstructive pattern with a FEV1 of 62% predicted and improving to 66% post-bronchodilator. Percutaneous aeroallergen skin testing was negative. Her initial labs demonstrated normal values for total IgE and eosinophils. The patient was started on high dose ICS/LABA to which she initially improved clinically and on spirometry with an FEV1 of 71%. She subsequently worsened both clinically and on spirometry and was stepped up to ICS/LABA/LAMA and next tezepelumab.

At her next scheduled appointment three months later, she reported only mild improvement in symptoms. Repeat spirometry showed no change in FEV1, remaining at 68% predicted after starting tezepelumab. At this point, the initial diagnosis of asthma was challenged. Methacholine challenge was negative. CT chest revealed a 1.9 cm mass adjacent to the right middle lobe bronchus, causing mass effect with 90% obstruction and narrowing of the lumen. She underwent a bronchoscopy with biopsy, which confirmed the diagnosis of an atypical pulmonary carcinoid tumor. She underwent a right lower lobectomy, and further imaging to rule out metastatic disease.

Conclusion: This case underscores the need to broaden the differential diagnosis and utilize all available diagnostic tools when common respiratory conditions like asthma fail to improve with appropriate treatment. Clinicians should promptly move to advanced imaging once the original differential diagnosis has been ruled out, to investigate other causes and avoid unnecessary delays in diagnosis. Early identification and confirmation through biopsy can expedite appropriate management and significantly improve patient prognosis and quality of life.

S8

COMFORT Toddlers: phase 3 supplemental safety study of epicutaneous immunotherapy in 1-through-3-year-old peanut-allergic toddlers

Julie Wang MD, Sara Anvari MD, Matthew Greenhawt MD, Douglas P. Mack MD, Sarita Chainani MS, Karine Rutault PhD, Katharine J. Bee PhD, Hugh A. Sampson MD

Introduction: The VIASKIN® peanut patch containing 250 µg peanut protein (VP250) is a novel approach to epicutaneous immunotherapy (EPIT), which aims to induce desensitization through the daily application of microgram amounts of peanut allergen to intact skin. In the 12-month, phase 3 EPITOPE trial, VP250 demonstrated a statistically significant treatment effect with a favorable safety profile in young children aged 1-3 years. The long-term, open-label extension (OLE) study, EPOPEX, showed further gains in treatment effect, and the placebo-crossover participants experienced a nearly identical treatment response after one year of treatment, demonstrating consistency of results. A supplemental safety study is planned to gather additional data to support the current safety profile of VP250 in this population.

Methods: The COMFORT Toddlers study is a phase 3, multicenter, randomized, double-blind, placebo-controlled trial in peanut-allergic toddlers aged 1-through-3 years. Key eligibility criteria include peanut-specific IgE >0.7kU$_A$/L, peanut skin prick test (SPT) ≥6 mm, and an eliciting dose (ED) ≤300 mg peanut protein at screening double-blind, placebo-controlled food challenge. Eligible participants will be randomized 3:1 to receive 6 months of VP250 or placebo, followed by an optional 18-month OLE study where all participants will receive VP250. Safety will be assessed throughout the study.

Results: Approximately 480 participants will be randomized. Safety assessments will include overall adverse events (AEs), local application site reactions, AEs of special interest, serious AEs, and AEs according to severity, duration, and relatedness to treatment. Additional assessments will include immunologic markers and patch user experience.

Conclusion: Previous VP250 phase 3 studies have demonstrated desensitization in children with a consistent and favorable safety profile. The COMFORT Toddlers study is designed to contribute to a robust safety dataset to support VP250 as a potential treatment option in young children with peanut allergy, if approved. Participant screening is anticipated to begin in Q2 2025.

Funding: DBV Technologies

S9

Time to End of Progression of Hereditary Angioedema Attacks Treated with Sebetralstat

Daniel F. Soteres MD, William R. Lumry MD, John Anderson MD, Jonathan A. Bernstein MD, Mauro Cancian MD, Danny M. Cohn MD, Henriette Farkas, Henry Li MD, James Hao PhD, Michael D. Smith PharmD, Paolo Bajcic MD, Paul K. Audhya MD, Markus Magerl MD

Introduction: On-demand treatments for hereditary angioedema (HAE) attacks aim to interdict the plasma kallikrein-kinin cascade and halt the progression of swelling. Stopping progression as early as possible after attack onset is important to minimize severity and reduce morbidity. This post hoc analysis examines the time to end of attack progression following treatment with sebetralstat in KONFIDENT-S (NCT05505916) and KONFIDENT (NCT05259917).

Methods: End of progression was defined as the time at which the worst attack severity was recorded using the 5-point Patient Global Impression of Severity (PGI-S) scale. PGI-S ratings (ranging from "very severe" to "none") were recorded by participants every 0.5 hours during the first 4 hours after taking sebetralstat, then every hour from 5 to 12 hours. This analysis includes attacks ranging from "none" to "very severe" at the time of treatment in the ongoing KONFIDENT-S open-label extension study (Sept 2024 cutoff) and Phase 3 KONFIDENT trial. Attacks with no post-baseline assessment were excluded.

Results: Analysis included 1591 attacks treated with 600mg sebetralstat from KONFIDENT-S and 84 attacks treated with 300mg sebetralstat and 88 attacks treated with 600mg sebetralstat from KONFIDENT. The median (interquartile range) time to end of progression within 4 hours of administration was 19.8 minutes (16.2-42.6) for attacks treated with 600mg sebetralstat in KONFIDENT-S, which was similar to 19.8 minutes (16.8-97.2) and 19.2 minutes (16.8-46.2) for attacks treated with 300mg and 600mg sebetralstat in KONFIDENT. In KONFIDENT-S, 90.3% of attacks treated with sebetralstat reached end of progression within 4 hours of administration, which was similar to KONFIDENT (82.1% of attacks treated with 300mg sebetralstat and 89.81% treated with 600mg sebetralstat).

Conclusions: In KONFIDENT-S, treatment with sebetralstat ended progression of HAE attacks early, with a median of 19.8 minutes, which was consistent with results from the KONFIDENT trial.

Funding: KalVista Pharmaceuticals

S10

On-demand Treatment of Hereditary Angioedema Attacks with Sebetralstat in Older Adults: Interim Analysis from KONFIDENT-S

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Introduction: Hereditary angioedema is a rare genetic disease associated with unpredictable attacks of tissue swelling, and older patients have reported an impact of age on disease burden. Here we present interim data on the safety and effectiveness of sebetralstat, an investigational oral on-demand therapy for attacks, in older adults (aged ≥65yrs) from the ongoing open-label KONFIDENT-S study (NCT05505916).

Methods: Participants were instructed to self-administer sebetralstat 600mg as early as possible for each attack, regardless of severity or anatomic location. Efficacy: time to beginning of symptom relief (Patient Global Impression of Change: at least "A Little Better" at ≥2 consecutive time points) within 12h; time to reduction in attack severity (Patient Global Impression of Severity [PGI-S]: improved rating at ≥2 consecutive time points) within 12h; time to complete attack resolution (PGI-S: "None") within 24h.

Results: As of September 14, 2024, 36 attacks (47.2% mild; 41.7% moderate; 8.3% severe) were treated with 1-2 administrations of sebetralstat by 4 participants aged ≥65yrs; baseline primary attack locations included 13 mucosal (36.1%, 1 laryngeal [2.8%]) and 33 subcutaneous (61.1%). Prior to enrollment participants aged ≥65yrs used on-demand treatment only to manage attacks (2 icatibant, 1 icatibant and/or C1INH, 1 unknown). Treatment-related adverse events occurred in 11 (9.9%) adults, including 1 in a participant ≥65yrs; no difficulty swallowing sebetralstat was reported. Median (IQR) time to treatment was 1.0min (1.0-2.0) and 15.0mins (1.0-75.0) for adults aged ≥65yrs and <65yrs. Median times to beginning of symptom relief were 1.87h (1.27-2.56) and 1.77h (0.88-5.30) for participants aged ≥65yrs and <65yrs. Of attacks reaching beginning of symptom relief within 12h (91.4%, ≥65yrs; 80.0%, <65yrs), 100% and 94.6% did so without an additional sebetralstat administration.

Conclusions: In this interim analysis of KONFIDENT-S, sebetralstat enabled rapid treatment, was well-tolerated, and demonstrated comparable effectiveness among adults aged ≥65 and <65 years.

Funding: KalVista Pharmaceuticals

S11

Dupilumab Induces Clinical Remission in Children With Uncontrolled, Effectiveness of Sebetralstat for Severe or Very Severe Hereditary Angioedema Attacks in KONFIDENT-S

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Introduction: Delayed treatment of hereditary angioedema (HAE) attacks is associated with increased attack severity and duration. Sebetralstat, an oral investigational plasma kallikrein inhibitor for on-demand treatment of HAE, enabled early treatment in the ongoing open-label extension KONFIDENT-S (NCT05505916) study. In this post hoc interim analysis, we evaluated the effectiveness of sebetralstat in the subset of attacks where administration was delayed and attacks had progressed in severity.

Methods: Effectiveness endpoints: time to beginning of symptom relief (Patient Global Impression of Change of at least "A Little Better" at ≥2 consecutive time points) within 12hrs; time to first reduction in severity from baseline (≥1 level decrease on the Patient Global Impression of Severity (PGI-S) scale at ≥2 consecutive time points) within 12hrs; time to complete attack resolution (PGI-S "None") within 24hrs. Time to substantial reduction of symptom burden was defined as time to PGI-S "Mild" for 2 consecutive time points within 24hrs. Delayed administration was defined as ≥1hr after attack onset.

Results: As of September 14, 2024, 30 participants (median age 29.0y, 67% female, 73% White, and 17% receiving long-term prophylaxis) treated 76 attacks rated severe or very severe with sebetralstat. Median (interquartile range [IQR]) time to treatment was 129.5 minutes (95.5-241.5). Forty-nine percent of attacks were mucosal (including 1 laryngeal) and 51% were subcutaneous. Median (IQR) time to beginning of symptom relief was 1.36hrs (0.76-3.97), time to reduction in attack severity was 1.77hrs (0.76-3.84), and time to complete attack resolution was >24hrs (11.08->24). Median time to substantial reduction of symptom burden was 9.15hrs (2.54->24) with 63.4% of attacks achieving the same within 24hrs.

Conclusion: In KONFIDENT-S, in the subset of attacks that were associated with delayed treatment and had progressed to severe or very severe, sebetralstat demonstrated early symptom relief and a rapid reduction in attack severity and symptom burden.

Funding: KalVista Pharmaceuticals

S12

Long-Term Prophylaxis Compliance and Healthcare Resource Utilization in Hereditary Angioedema: A Claims Database Analysis

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Introduction: Multiple non-androgen long-term prophylaxis (LTP) therapies have been approved in the US for prophylaxis of attacks of hereditary angioedema (HAE). Up to date real-world data on compliance, healthcare resource utilization (HRU) and costs in this population are limited. This study assessed LTP refill patterns, associated HRU and costs in patients with HAE using a national claims database.

Methods: Commercially-insured patients from the IQVIA PharMetrics® Plus database (January 2016–September 2023) had ≥1 claim for non-androgen LTP, with ≥6 months of continuous enrollment before and ≥12 months post-index (first LTP claim). Patient cohorts: no/minimal refill gaps, with refill gaps, or switchers. Annualized mean on-demand therapy claims, HRU, and costs were evaluated 12 months pre- and post-index.

Results: Most patients (220/328) had ≥1 post-index on-demand therapy claim. Mean (SD) annualized on-demand therapy doses pre- and post-LTP, respectively, were 20.8 (25.1) vs 12.4 (15.2) (P=0.001) with no/minimal refill gaps (n=147), 18.3 (19.7) vs 18.0 (22.3) (P=0.769) with refill gaps (n=131), and 25.7 (28.7) vs 29.2 (28.8) (P=0.12) for switchers (n=50). During 1-year follow-up, 17% had ≥1 HAE-related ER visit claim and 8% had ≥1 HAE-related inpatient visit. Mean annualized total HAE-related healthcare cost per patient per year were $165,348 pre-LTP and $515,333 post-LTP, driven by LTP pharmacy costs (mean $395,845 PPPY), and partially offset by reductions in medical costs (ER/In-patient, mean $8,344 PPPY).

Conclusions: High frequency of administration has been reported as a challenge associated with LTP, this study found 55% of LTP patients had substantial refill gaps in their LTP claims, discontinued, or switched within a year from initiation. Substantial increases in total HAE-related healthcare costs were observed, driven by LTP pharmacy costs without significant reductions in HRU.

Funding: KalVista Pharmaceuticals

S16

Rocatinlimab Significantly Improved Clinical Signs and Symptoms by Targeting OX40R+ T cells in Patients with Moderate-to-Severe Atopic Dermatitis: Results from the Phase 3 ROCKET-Horizon Trial

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Introduction: Rocatinlimab (AMG 451/KHK4083), a first-in-class T-cell rebalancing therapy, inhibits and reduces pathogenic T cells by targeting the OX40 receptor (OX40R). The multicenter, randomized, double-blind ROCKET-Horizon trial (NCT05651711) evaluated the efficacy and safety of rocatinlimab monotherapy vs placebo in adults with moderate-to-severe atopic dermatitis and inadequate topical medication response.

Methods: A total of 726 adults ≥18 years old were randomized 3:1 to subcutaneous rocatinlimab 300 mg every 4 weeks (plus loading dose at week 2) or placebo for 24 weeks. Co-primary endpoints were ≥75% reduction in Eczema Area and Severity Index from baseline (EASI-75) and validated Investigator Global Assessment for atopic dermatitis (vIGA-AD™) 0/1 with ≥2-point baseline reduction at week 24. Rescue therapy was permitted from Day 1. The primary analysis considered rescue therapy users and patients with missing data as nonresponders. A prespecified sensitivity analysis was conducted regardless of rescue use.

Results: Study met its co-primary endpoints at week 24: EASI-75 response was 32.8% for rocatinlimab vs 13.7% for placebo (P<0.001); vIGA-AD 0/1 response was 19.3% for rocatinlimab vs 6.6% for placebo (P<0.001). The prespecified sensitivity analysis allowing rescue use demonstrated greater improvement at week 24 for rocatinlimab vs placebo (EASI-75, 46.6% vs 15.8% [P<0.001]; vIGA-AD 0/1, 24.1% vs 6.6% [P<0.001]). Rocatinlimab depth-of-skin response did not plateau at week 24. All key secondary endpoints were met, including ≥90% reduction in EASI from baseline (EASI-90) and ≥4-point reduction in worst pruritus numerical rating scale at week 24. Rocatinlimab specifically reduced OX40R+ T cells and was generally well-tolerated.

Conclusions: Rocatinlimab significantly improved clinical manifestations in the primary analysis (and even more in the prespecified sensitivity analysis allowing rescue use), rebalancing T cells by specifically reducing OX40R+ T cells while maintaining the overall T-cell population. This potentially provides a unique avenue to treat and modify the atopic dermatitis disease course.

Funding: **Amgen Inc. and Kyowa Kirin Co., Ltd**

S17

Reduction in Asthma Exacerbations Following Initiation of Benralizumab Among Medicare Beneficiaries: Results from the ZEPHYR-5 Study

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Introduction: This real-world evidence study sought to evaluate the change in asthma exacerbations following initiation of benralizumab among older patients, who are typically underrepresented in clinical trials and retrospective studies.

Methods: Medicare Fee-for-Service (MFFS) and Medicare Advantage (MA) claims spanning 2017-2022 were utilized for this study. Inclusion criteria: 1) prescription for benralizumab and ≥1 refill within 90 days (earliest prescription=index date), 2) 12 months of enrollment with MFFS or MA benefits preceding (baseline) and following (follow-up) the index date, 3) ≥1 inpatient or ≥2 outpatient claims with a diagnosis code for asthma during the baseline period, and 4) presence of ≥2 asthma exacerbations during the baseline period. Exacerbations were assessed during the baseline and follow-up periods, and were defined as 1) an asthma-related hospitalization, 2) a mechanical ventilation claim, or 3) an outpatient or emergency department visit with an asthma diagnosis and a claim for systemic corticosteroids within seven days. Percent change in annual asthma exacerbation rate (AAER) was assessed from the baseline to follow-up.

Results: 4,611 patients qualified for the study. The mean±SD age was 69.3±10.9, and the majority were female sex (n=3,185; 69.1%) and MFFS beneficiaries (n=4,213; 91.4%). There was a 43.5% reduction in the AAER from the baseline period to the follow-up period (3.8±2.0 to 2.2±2.2 exacerbations per year; $p < 0.001$). The proportion of patients with ≥4 exacerbations decreased 50.5%.

Conclusions: Older patients with severe asthma treated with benralizumab demonstrated meaningful reductions in the rate of asthma exacerbations in a real-world setting.

Funding: AstraZeneca

S18

Lung Function Improvement in Patients with Uncontrolled, Moderate-to-severe Asthma Treated with Benralizumab: A New, Retrospective Analysis of the Pooled SIROCCO and CALIMA Studies

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Introduction: Airway remodeling in severe asthma leads to progressive loss of lung function and incomplete reversibility of airflow obstruction. We examined the effect of benralizumab on lung function in the SIROCCO and CALIMA studies utilizing a new analysis of spirometry.

Methods: This retrospective analysis pooled data from two randomized, placebo-controlled, Phase 3 studies: SIROCCO (48 weeks; patients with severe asthma) and CALIMA (56 weeks; patients with moderate-to-severe asthma). Patients (aged 12–75 years) had ≥2 exacerbations in the previous year despite medium- to high-dose inhaled corticosteroids plus additional controllers. Patients were stratified (2:1) by baseline blood eosinophils (bEOS) ≥300 cells/μL or <300 cells/μL. In this analysis, patients receiving subcutaneous benralizumab 30 mg every 8 weeks (first three doses every 4 weeks) were assessed for changes in pre- and post-bronchodilator forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) at baseline and study end.

Results: In total, 839 patients received benralizumab: bEOS ≥300 cells/μL, n=557; bEOS <300 cells/μL, n=282. In the overall population, mean (standard deviation) pre- and post-bronchodilator FEV_1 at baseline were 1722 (615) mL and 2128 (755) mL. Pre- and post-bronchodilator FEV_1 at study end were 2029 (756) mL and 2225 (800) mL. Pre- and post-bronchodilator FVC at baseline were 2865 (905) mL and 3285 (971) mL. Pre- and post-bronchodilator FVC at study end were 3214 (1010) mL and 3379 (1021) mL. Pre-bronchodilator FEV_1 and FVC improved by 307 mL and 349 mL and post-bronchodilator FEV_1 and FVC improved by 97 mL and 94 mL between baseline and study end, respectively. Stratified by bEOS, findings were similar in both groups.

Conclusions: Benralizumab improved FEV_1 and FVC while maintaining bronchodilator response in patients with uncontrolled, moderate-to-severe asthma, irrespective of bEOS, potentially reflecting reduced hyperinflation due to improved airway inflammation and mucus plugging.

Funding: AstraZeneca

S19

Lebrikizumab Improves Atopic Dermatitis in Adult and Adolescent Patients with Skin of Color: 16-week Results from the ADmirable Study

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Introduction: We report the first primary results of any Phase 3 clinical trial studying patients with atopic dermatitis (AD) and skin of color (SoC).

Methods: At baseline and Week-2, patients received 500-mg lebrikizumab loading doses followed by 250-mg every 2 weeks through Week-16. Concomitant topical therapy was allowed. Patients receiving protocol-defined rescue therapy were discontinued. Key eligibility criteria included: ≥12 years of age, self-reported race other than White, Fitzpatrick Phototype IV-VI, and moderate-to-severe AD. Endpoints are summarized as observed and using non-responder imputation/multiple imputation (NRI/MI; supporting analysis).

Results: At baseline (N=90), patients had a mean (SD) age of 40.7 (19.6) years, AD disease duration of 19.7 (16.1) years, EASI 26.4 (12.2), and Pruritus Numeric Rating Scale (NRS) of 7.0 (2.2). 43% patients were female and 16% were adolescent. Most patients had an IGA of 3 (69%). 78% patients self-reported their race as Black/African American. Patients had Fitzpatrick Phototypes of IV (43%), V (24%), and VI (32%). At Week-16, 69.2% (54/78) of patients achieved a 75% improvement in EASI (NRI/MI, 66.9%), 44.9% (35/78) achieved a 90% improvement in EASI (NRI/MI, 42.5%), 44.9% (35/78) achieved an IGA 0/1 with ≥2-point improvement (NRI/MI, 44.1%), and 58.1% (36/62) reported ≥4-point Pruritus NRS improvement (NRI/MI, 55.4%). Hypopigmentation and hyperpigmentation improved in 33.3% (4/12) and 63.0% (29/46) of patients, respectively (as observed). Most treatment emergent adverse events were mild-to-moderate in severity.

Conclusion: Lebrikizumab improved signs and symptoms of disease, including post-inflammatory pigment discoloration, in patients with AD and SoC and demonstrated a favorable safety profile.

Funding: Dermira, subsidiary of Eli Lilly and Company

S20

Maintenance of Lebrikizumab Efficacy in Patients With Moderate-To-Severe Atopic Dermatitis and Atopic Comorbidities

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Introduction: 52-week lebrikizumab (LEB) efficacy was assessed in adult and adolescent patients with moderate-to-severe atopic dermatitis (AD) with or without atopic comorbidities using data pooled from monotherapy studies, ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967).

Methods: Patients responding to LEB every 2 weeks (LEBQ2W) at the end of the 16-week induction period were re-randomized to receive LEBQ2W, LEB every 4 weeks (LEBQ4W), or placebo (withdrawal) for 36 additional weeks. 52-week efficacy was assessed with Investigator's Global Assessment score of 0 or 1 (IGA 0/1), 75% improvement in the Eczema Area and Severity Index (EASI75), and ≥4-point improvement on the Pruritus numeric rating scale (NRS) by patients with or without atopic comorbidity. Data were set to non-responders after systemic rescue, lack-of-efficacy discontinuation, or escape-arm transfer or set to missing after topical use or discontinuation for other reasons. Multiple imputation was used for missing data. Logistic regression was performed with treatment, study, subgroup, and subgroup-by-treatment interaction at Week 52.

Results: Among patients with ≥1 or no atopic comorbidities at Week 52, respectively, the proportions of patients(N) with IGA 0/1 were: 80%(55), 70%(22) for LEBQ4W; 68%(53), 78%(24) for LEBQ2W; 38%(28), 76%(10) for withdrawal; EASI75 were 83%(86), 79%(29) for LEBQ4W; 79%(78), 78%(34) for LEBQ2W; 64%(43), 75%(14) for withdrawal; and Pruritus NRS improvement were 81%(48), 94%(17) for LEBQ4W; 84%(44), 87%(17) for LEBQ2W; 69%(21), 58%(7) for withdrawal. LEB responses were similar for patients with and without atopic comorbidities.

Conclusion: LEB efficacy was maintained through 52 weeks in patients with moderate-to-severe AD with and without atopic comorbidities**.**

Funding: Dermira, subsidiary of Eli Lilly and Company

S21

Long-term Efficacy and Safety of Lebrikizumab is Maintained in Patients With Moderate-to-Severe Atopic Dermatitis: Results Up To 3 Years From ADjoin

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Introduction: Lebrikizumab (LEB), a monoclonal antibody with high-affinity to IL-13, has demonstrated efficacy and safety in atopic dermatitis (AD) phase 3 clinical trials. We report LEB efficacy and safety in long-term extension study ADjoin following up to 152 Weeks (W) of continuous LEB treatment with/without TCS.

Methods: ADvocate1&2 patients (pts) who achieved per-protocol response (EASI75 or IGA 0/1 without TCS) following 16W LEB treatment were re-randomized 2:2:1 to LEB 250mg Q2W, Q4W, or placebo (withdrawal). ADvocate1&2 pts who completed W52 and ADhere pts who completed W16 could enroll into ADjoin; LEB responders were randomized 2:1 to LEB 250mg Q2W or Q4W. Data are reported for W16 LEB responders from ADvocate1&2 (N=181) and ADhere (N=86) who received LEB 250mg Q2W or Q4W in ADjoin. Efficacy outcomes were assessed (as observed analysis) up to ADjoin W100 (total 152W and 116W of LEB treatment from ADvocate1&2 and ADhere, respectively).

Results: In ADvocate1&2 pts, at W152 IGA 0/1 was maintained by 82.9% (34/41; Q2W) and 84.0% (42/50; Q4W) and EASI75 by 90.5% (57/63; Q2W) and 94.1% (64/68; Q4W). In ADhere pts, at W116 IGA 0/1 was maintained by 86.7% (26/30; Q2W) and 91.7% (11/12; Q4W) and EASI75 by 94.9% (37/39; Q2W) and 90.9% (20/22; Q4W). EASI90 was reported by 79.4% (50/63; Q2W) and 86.8% (59/68; Q4W) of ADvocate1&2 pts and 84.6% (33/39; Q2W) and 86.4% (19/22; Q4W) of ADhere pts. ADjoin adverse events (AE): 29.2% (78/267) mild, 33.3% (n=89) moderate and 3.7% (n=10) serious; 2.6% (n=7) reported treatment discontinuation due to AEs.

Conclusion: Efficacy outcomes were maintained up to 3 years of continuous LEB treatment, in both LEB 250mg Q2W and Q4W arms. The LEB safety profile in ADjoin was consistent with previous LEB studies on moderate-to-severe AD.

Funding: Dermira, subsidiary of Eli Lilly and Company

S22

Key Treatment Attributes and Preferences of Allergists and Dermatologists for Moderate-To-Severe Atopic Dermatitis: Results from a US-Based Real-World, Cross-Sectional Study

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Introduction: Despite the availability of multiple novel targeted therapies for atopic dermatitis (AD), key treatment attributes influencing physician preferences are not well understood. We explored treatment attribute preferences and strategies for moderate-to-severe AD among allergists and dermatologists.

Methods: Data were drawn from Adelphi AD Disease Specific Programme™, cross-sectional survey of US-based physicians (Oct'22–Mar'23). Physicians rated importance of treatment attributes in managing moderate-to-severe AD (scale 1–5: 1='not important'; 5='extremely important'), stated which treatments they typically used at first/second/third-line, and how they perceived oral JAK inhibitors (JAKi) versus biologics. Data are summarized descriptively.

Results: Allergists (n=19) and dermatologists (n=70) similarly rated several treatment attributes as extremely important: relief from pruritus (79%;70%); improvement of skin lesions (68%;63%), pain/soreness/discomfort (68%;60%) and achieving clear skin (47%;46%). Numerically, more allergists (versus dermatologists) rated reducing sleep disruption (89%;57%) and flares (84%;59%); long-term control (84%;64%) and safety (84%;61%); controlling skin infection (74%;49%); affordability (68%;46%); and sustained efficacy (63%;47%) as extremely important. Preferred treatment placement for severe AD varied between allergists and dermatologists (first-line: emollients [79%;50%], antihistamines [58%;36%], topical corticosteroids (TCS) [moderate-potency:58%;44%; high-potency:47%;67%]; second-line: high-potency TCS [32%;29%], biologics [32%;49%], topical JAKi [16%;40%]; third-line: biologics [63%;53%], Oral JAKi [58%;63%], systemic immunosuppressants [42%;27%]). Overall treatment perception of oral JAKi versus biologics varied amongst allergists and dermatologists (much/somewhat worse [47%;29%], equivalent [37%;39%], somewhat/much better [16%;33%]).

Conclusion: Specialists' preferences for treatment attributes and strategies, and perceptions of different advanced systemic therapies for moderate-to-severe AD, varied. Further data are needed to assess whether preferences/perceptions of advanced systemics change, and influence prescribing decisions as new treatments become available.

Funding: Eli Lilly and Company

S23

Albuterol-Budesonide Treatment in Acute Airway Obstruction: Patient Selection for the ALTA Study

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Introduction: The *AL*buterol-budesonide *T*reatment in *A*cute airway obstruction (ALTA) study (NCT05555290) will assess efficacy, safety, and mechanisms of action of albuterol-budesonide 180/160 µg versus albuterol 180 µg in treating and preventing bronchoconstriction. This report describes the clinical profiles of patients meeting criteria for randomization into the trial.

Methods: ALTA is a phase 3b, randomized, double-blind, cross-over study evaluating the effects of repetitive dosing of albuterol-budesonide 180/160 µg versus albuterol 180 µg for adults treated as intermittent asthma and experiencing acute airway obstruction induced by repeated mannitol challenges. Inclusion criteria include asthma diagnosis ≥6 months, prescribed and utilizing albuterol as the only asthma treatment for ≥4 weeks, pre-bronchodilator $FEV_1 \geq 1.50$ L and $FEV_1 \geq 60\%$ to < 90% predicted, and positive response to a mannitol challenge (decrease in $FEV_1 \geq 15\%$ at ≤ 635 mg cumulative mannitol dose). Exclusion criteria include clinically significant lung disease other than asthma; smoking in the prior 6 months or ≥10 pack-year smoking history; or a clinical encounter for asthma worsening within the past 4 weeks.

Results: Thus far, 84 patients have met the criteria for randomization into ALTA. Mean(SD) age=44.9(13.7) years, 56.0% female, 40.5% African American, 9.5% Hispanic/Latino. Clinical characteristics include 10.7% with 1 prior-year severe exacerbation; mean(SD) fractional exhaled nitric oxide=37.0(37.4) ppb; mean(SD) baseline pre-bronchodilator FEV_1=2.464(0.538) L; mean(SD) baseline percent predicted FEV_1=76.7(7.9)%; mean(SD) % fall in FEV_1 with mannitol challenge=22.1(7.3)% at a mean(SD) cumulative mannitol dose of 146.4(176.3) mg. No patients met NAEPP 2007 criteria for intermittent disease, and 13.1% fell into the mild, 78.6% moderate, and 8.3% severe persistent asthma categories. As measured by the Asthma Impairment and Risk Questionnaire, 60.7% had well-controlled, 20.2% not well-controlled, and 19.1% very poorly controlled disease.

Conclusion: Patients treated as intermittent asthma exhibit heterogeneity in clinical characteristics, airway hyper-reactivity, T2 inflammation, and disease severity and control.

Funding: AstraZeneca

S24

Performance of the Pediatric Asthma Impairment and Risk Questionnaire (Peds-AIRQ) in Assessing Control for Children with Asthma Aged 5 to 11 Years

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Introduction: Asthma control is often overestimated in clinical practice because exacerbation history may not be considered. Almost half of US children with asthma aged 5-11 years have uncontrolled disease, placing them at risk for exacerbations. The Peds-AIRQ was validated against a standard of GINA symptom control (impairment) and prior-year exacerbations (risk) and offers an equally weighted, 8-item (5 impairment, 3 risk), yes/no control tool for children aged 5-11 years (well-controlled 0-1, not well-controlled 2-4, very poorly controlled 5-8 yes responses). We compared Peds-AIRQ with other assessments in categorizing control for children relative to prior-year exacerbations.

Methods: Control assessments by C-ACT (well-controlled, not well-controlled, very poorly controlled) and parent/caregiver impression and physician opinion (controlled, well-controlled, somewhat-controlled, poorly controlled, not-controlled) were obtained for children aged 5-11 years enrolled in the Peds-AIRQ validation study. Physician opinion was informed by clinic visit (history, physical examination, chart review of medications and prior-year exacerbations). Chi-square and McNemar's test compared proportions of children with prior-year exacerbations assessed as completely/well-controlled and uncontrolled (not well-, somewhat-, poorly, very poorly, and not-controlled) by each assessment measure versus Peds-AIRQ, overall and by age subgroup (5-6, 7-8, and 9-11 years); significance $P \leq 0.05$.

Results: 399 children were included: mean(SD) age 7.9(1.9) years (n=107 5-6-year-olds, 136 7-8-year-olds, 156 9-11-year-olds); 63% male; 69% White, 15% self-reported Black/Black-mixed race; 33% self-reported Hispanic/Latino ethnicity; 39% public insurance. Overall, 45.9% experienced ≥1 prior-year exacerbation (5-6-year-olds: 48.6%, 7-8-year-olds: 49.3%; 9-11-year-olds: 41%, P=0.30). Peds-AIRQ identified a lower proportion of children as well-controlled (39.8%) vs C-ACT (69.2%), physicians (64.9%), and parent/caregivers (71.9%); P <0.001. Peds-AIRQ classified the lowest proportion of children with prior-year exacerbations as well-controlled (20.8% vs C-ACT: 39.1%, physicians: 32.0%, parents/caregivers: 36.9%; P <0.001). No differences were observed across age subgroups within any of these assessments. For the total population, Peds-AIRQ identified the lowest proportion as well-controlled and the highest proportion as uncontrolled among those who experienced ≥1 or ≥2 prior-year exacerbations (well-controlled Peds-AIRQ vs other assessments: 8% vs 20-27% for ≥1, 5% vs 14-18% for ≥2; uncontrolled Peds-AIRQ vs other assessments: 38% vs 18-25% for ≥1, 29% vs 16-20% for ≥2; P<0.001 for all comparisons).

Conclusions: Compared with C-ACT, physician opinion, and parent/caregiver impression, Peds-AIRQ is least likely to assess children with prior-year exacerbations as well-controlled and most likely to identify those with an exacerbation history as uncontrolled. At point-of-care, Peds-AIRQ can help identify children who may benefit from optimization of their asthma management.

Funding: AstraZeneca

S25

Two-Year Efficacy and Safety of Benralizumab in the Treatment of Eosinophilic Granulomatosis with Polyangiitis

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Introduction: The double-blind period of the MANDARA trial (NCT04157348) demonstrated non-inferiority of benralizumab to mepolizumab for remission, in adults with eosinophilic granulomatosis with polyangiitis (EGPA). Here, we report the 2-year combined double-blind and ongoing open-label extension (OLE) data.

Methods: Patients who completed the 52-week double-blind, entered the OLE where they continued benralizumab (benra/benra; n=66) or switched from mepolizumab to benralizumab (mepo/benra; n=62). Endpoints included remission (Birmingham Vasculitis Activity Score=0 and oral glucocorticoid [OGC] dose ≤4 mg/day), OGC use, relapse, blood eosinophil count (bEOS), Asthma Control Questionnaire (ACQ-6), pre-bronchodilator forced expiratory volume in 1 second (pre-BD FEV1), and safety.

Results: At Week 104, 41 [62.1%] benra/benra and 42 [67.7%] mepo/benra patients achieved remission. During the OLE, 51 (77.3%) benra/benra and 42 (67.7%) mepo/benra patients had no relapses. At Weeks 49–52, 27 (40.9%) benra/benra and 16 (25.8%) mepo/benra patients had withdrawn OGCs, increasing to 29 (43.9%) and 27 (43.5%) at Weeks 101–104 in the OLE. The median (IQR) bEOS in benra/benra patients was 20 (10,40) cells/μL at both Weeks 52 and 100; bEOS were depleted in mepo/benra patients from 70 (40,90) cells/μL to 20 (10,50) cells/μL by 4 weeks after switching. Mean (SD) ACQ-6 scores were 0.64 (0.78) in benra/benra and 0.60 (0.76) in mepo/benra patients at Week 104 versus 1.39 (1.18) and 1.11 (0.95) at baseline. Mean (SD) pre-BD FEV1 was 2.59 (0.90) L versus 2.62 (0.84) L in benra/benra versus mepo/benra patients at Week 52, and 2.61 (0.90) versus 2.63 (0.81) L, at Week 100. Safety was consistent with the benralizumab profile.

Conclusions: In EGPA patients receiving benralizumab, remission rates, OGC discontinuation, and bEOS depletion were durable over 104 weeks with low relapse rates, without loss of asthma control, or lung function decline. Additional bEOS depletion and OGC sparing was observed in patients switching from mepolizumab to benralizumab.

Funding: AstraZeneca

S26

Dupilumab is Efficacious in Children (Aged 1 to <12 Years) With Eosinophilic Esophagitis Regardless of Prior History of Comorbidities

Jonathan M. Spergel, MD, Evan S. Dellon, MD, Changming Xia, PhD, Bram P. Raphael, MD, Juby A. Jacob-Nara, MD, Amr Radwan, MA

Introduction. Eosinophilic esophagitis (EoE) is a chronic, progressive, type 2 inflammatory disease impacting quality of life. EoE KIDS (NCT04394351) evaluated dupilumab in children (1 to <12 years) with EoE. Type 2 comorbidities are common in patients with EoE; therefore, this post-hoc analysis assessed dupilumab efficacy in children according to prior history of common comorbidities in EoE.

Methods. This EoE KIDS analysis focused on patients randomized to higher-exposure dupilumab (weight-tiered dosing) or placebo for 16 weeks (W). Endpoints included rate differences (dupilumab vs placebo) in the proportion achieving peak intraepithelial eosinophil count (PEC) ≤6 eosinophils/high-power field (eos/hpf; primary endpoint) and <15 eos/hpf, and mean changes in Endoscopic Reference Score (EREFS), Histologic Scoring System (HSS) grade/stage scores, and Pediatric EoE Sign/Symptom Questionnaire–Caregiver version (PESQ-C); endpoints were stratified by prior history of atopic dermatitis (AD), asthma, and allergic rhinitis (AR).

Results. Of 71 children, 97.2% had a current comorbid atopic/allergic condition; 43 had prior history of AD (dupilumab/placebo, n=21/22), 39 had asthma (n=24/15), and 51 had AR (n=29/22). At W16, dupilumab led to greater proportions achieving PEC ≤6 eos/hpf (rate difference vs placebo [95% CI]: AD: yes 71.4% [52.1, 90.8], no 54.2% [25.8, 82.6]; asthma: yes 55.8% [32.7, 79.0], no 76.9% [54.0, 99.8]; AR: yes 64.4% [45.5, 83.4], no 62.5 [29.0, 96.1]; **Table**) and <15 eos/hpf vs placebo, irrespective of common comorbidities. Dupilumab improved EREFS and HSS grade/stage scores vs placebo in all subgroups at W16 (**Table**). Dupilumab treatment generally led to a reduced proportion of days with ≥1 EoE sign (measured by PESQ-C) vs placebo at W16, with some variability across comorbidities (**Table**).

Conclusion: Dupilumab at a higher-exposure regimen improved features of EoE vs placebo, in children (aged 1 to <12 years) with or without past medical history of AD, asthma, and AR.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

S27

Dupilumab improves histologic, symptomatic, and endoscopic outcomes in children with eosinophilic esophagitis in the EoE KIDS study, regardless of history of elimination diet or concomitant food allergy

Jonathan M. Spergel, MD, Antonella Cianferoni, MD, Mirna Chehade, MD, Changming Xia, PhD, Lacey Robinson, MD, Jennifer Maloney, MD, Margee Louisias, MD, Allen Radin, MD

Introduction: Food elimination diets may be effective at improving eosinophilic esophagitis (EoE) symptoms; however, may be difficult to follow and reduce quality of life. This analysis assessed dupilumab efficacy in children with EoE with/without a history of food elimination diet and concomitant food allergy at baseline in the Phase 3 EoE KIDS study.

Methods: Eligible patients were aged 1 to <12 years with EoE unresponsive to proton-pump inhibitors. In Part A, patients were randomized to weight-tiered dupilumab higher-exposure (HE) or placebo (two groups), through to Week (W) 16. In Part B, patients receiving dupilumab HE continued the same regimen, and patients in placebo groups switched to dupilumab HE through to W52. Participants on a food elimination diet at baseline remained on the same diet throughout. Efficacy was assessed by history of food elimination diet and concomitant food allergy at W16 and W52.

Results: Of 102 patients, most (88.2%) had a history of food elimination diets and 82.4% had a concomitant food allergy at baseline. At W16, proportion of patients with ≤6 eosinophils per high-power field in patients with/without a history of elimination diet was 69.7%/50.0% with dupilumab HE and 3.3%/0% with placebo; in patients with/without food allergy at baseline, proportions were 67.7%/66.7% with dupilumab HE and 3.6%/0% with placebo. Generally, improvements in histologic, endoscopic, and symptomatic outcomes were observed across patients regardless of history of food elimination diet or concomitant food allergy, although patient numbers were small. Efficacy was maintained at W52 with dupilumab HE, while improvements were observed in patients who switched from placebo to dupilumab HE at W16. Dupilumab demonstrated an acceptable safety profile.

Conclusion: Dupilumab HE showed sustained improvements in histologic, symptomatic, and endoscopic aspects of EoE regardless of history of food elimination diet or concomitant food allergy.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

S28

Dupilumab Efficacy in Pooled LIBERTY-CSU CUPID Study A and Study C Regardless of Baseline Total Serum IgE Levels

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Introduction: Chronic spontaneous urticaria (CSU) is a chronic inflammatory skin disease characterized by pruritic wheals with or without angioedema. Many patients have an inadequate response to current therapies, which may be informed by total serum IgE levels.

Methods: LIBERTY-CSU CUPID Study A and Study C (NCT04180488) were replicate, 24-week, randomized, double-blind, placebo-controlled, phase 3 trials of dupilumab treatment in omalizumab-naïve patients aged ≥6 years with symptomatic CSU despite standard-of-care H1-antihistamine treatment (≤4-fold the approved dose). Patients were randomized to receive add-on dupilumab (pooled: 144 patients) 300 mg (adults, adolescents: ≥60 kg) or 200 mg (adolescents: <60 kg, children: ≥30 kg) or matched placebo (pooled: 145 patients) subcutaneously every 2 weeks. Efficacy endpoints included Itch Severity Score over 7 days (ISS7; range 0–21) and Urticaria Activity Score over 7 days (UAS7; range 0–42) at Week 24 in patients with baseline serum total IgE above and below 40, 60, or 103 IU/mL. Safety was also assessed.

Results: Dupilumab treatment improved itch and urticaria activity at Week 24, regardless of baseline serum IgE levels. Least squares mean change from baseline (dupilumab vs placebo) in ISS7 was IgE <40 IU/mL: −12.1 vs −7.7, ≥40 IU/mL: −9.6 vs −6.0, <60 IU/mL: −10.8 vs −7.0, ≥60 IU/mL: −9.8 vs −6.1, <103 IU/mL: −10.5 vs −6.2, and ≥103 IU/mL: −10.1 vs −7.3, and in UAS7 was IgE <40 IU/mL: −23.1 vs −14.7, ≥40 IU/mL: −18.6 vs −11.6, <60 IU/mL: −20.1 vs −13.0, ≥60 IU/mL: −19.3 vs −12.0, <103 IU/mL: −19.9 vs −12.0, and ≥103 IU/mL: −19.3 vs −13.7 (nominal *P* for interactions >0.05). The occurrence of treatment-emergent adverse events (dupilumab vs placebo) was 53.5% vs 55.9%. Overall safety was generally consistent with the known dupilumab safety profile.

Conclusions: Dupilumab demonstrated consistent improvement in CSU signs and symptoms, regardless of serum total IgE levels.

Funding: Sanofi and Regeneron Pharmaceuticals Inc. (NCT04180488)

S29

Dupilumab Provides Early and Sustained Improvement in Itch in Patients With Chronic Spontaneous Urticaria: Pooled Results From LIBERTY-CSU CUPID Study A and Study C

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Introduction: Chronic spontaneous urticaria (CSU) is a chronic inflammatory skin disease characterized by wheals with or without angioedema, with associated itch and burning that adversely impact patients' quality of life. Dupilumab, an interleukin (IL)-4/IL-13 inhibitor, has demonstrated improvement in itch in antihistamine-resistant omalizumab-naïve patients with CSU in LIBERTY-CSU CUPID Study A. Here, we assessed the efficacy of dupilumab vs placebo on itch severity over time in a pooled analysis of the replicate studies CUPID Study A and CUPID Study C.

Methods: LIBERTY-CSU CUPID Study A and Study C (NCT04180488) were replicate, 24-week, randomized, double-blind, placebo-controlled, phase 3 trials of dupilumab treatment in omalizumab-naïve patients aged ≥6 years with symptomatic CSU despite standard-of-care H1-antihistamine treatment (≤4-fold the approved dose). Patients were randomized to receive add-on dupilumab (pooled: 144 patients) 300 mg (adults, adolescents: ≥60 kg) or 200 mg (adolescents: <60 kg, children: ≥30 kg) or matched placebo (pooled: 145 patients) subcutaneously every 2 weeks. Efficacy endpoints included change from baseline in Itch Severity Score over 7 days (ISS7; range 0–21) over time, from baseline to Week 24. All *P* values were nominal, with no adjustments for multiple testing.

Results: Dupilumab improved itch (ISS7) over time compared with placebo starting from Week 3 (least squares mean [standard error] change from baseline: dupilumab, −5.0 [0.5]; placebo, −3.6 [0.5]; nominal $P = 0.0153$) through Week 24 (dupilumab, −9.9 [0.7]; placebo, −6.7 [0.7]; nominal $P < 0.0001$). The occurrence of treatment-emergent adverse events (dupilumab vs placebo) was 53.5% vs 55.9%. Overall safety was generally consistent with the known dupilumab safety profile.

Conclusions: Dupilumab demonstrated early and sustained improvements in itch starting from Week 3, supporting dupilumab as a treatment for antihistamine-resistant CSU.

Funding: Sanofi and Regeneron Pharmaceuticals Inc. (NCT04180488)

S30

Dupilumab Provides Early and Sustained Improvement in Urticaria Activity in Patients With Chronic Spontaneous Urticaria: Pooled Results From LIBERTY-CSU CUPID Study A and Study C

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Introduction: Chronic spontaneous urticaria (CSU) is a chronic inflammatory skin disease characterized by wheals with or without angioedema, with associated itch and burning that adversely impact patients' quality of life. Dupilumab, an interleukin (IL)-4/IL-13 inhibitor, has demonstrated improvement in urticaria activity in antihistamine-resistant, omalizumab-naïve patients with CSU in LIBERTY-CSU CUPID Study A. Here, we assessed the efficacy of dupilumab vs placebo on urticaria activity over time in a pooled analysis of the replicate studies CUPID Study A and CUPID Study C.

Methods: LIBERTY-CSU CUPID Study A and Study C (NCT04180488) were replicate, 24-week, randomized, double-blind, placebo-controlled, phase 3 trials of dupilumab treatment in omalizumab-naïve patients aged ≥6 years with symptomatic CSU despite standard-of-care H1-antihistamine treatment (≤4-fold the approved dose). Patients were randomized to receive add-on dupilumab (pooled: 144 patients) 300 mg (adults, adolescents: ≥60 kg) or 200 mg (adolescents: <60 kg, children: ≥30 kg) or matched placebo (pooled: 145 patients) subcutaneously every 2 weeks. Efficacy endpoints included change from baseline in Urticaria Activity Score over 7 days (UAS7; range 0–42) over time, from baseline to Week 24. All *P* values were nominal, with no adjustments for multiple testing.

Results: Dupilumab improved urticaria activity (UAS7) over time compared with placebo, starting from Week 3 (least squares mean [standard error] change from baseline: dupilumab, −9.9 [0.9]; placebo, −6.9 [0.9]; nominal $P = 0.0066$) through Week 24 (dupilumab, −19.3 [1.3]; placebo, −13.1 [1.3]; nominal $P < 0.0001$). The occurrence of treatment-emergent adverse events (dupilumab vs placebo) was 53.5% vs 55.9%. Overall safety was generally consistent with the known dupilumab safety profile.

Conclusions: Dupilumab demonstrated early and sustained improvements in urticaria activity starting from Week 3, supporting dupilumab as a treatment for H1-antihistamine-resistant CSU.

Funding: Sanofi and Regeneron Pharmaceuticals Inc. (NCT04180488)

S31

Efficacy and Safety Results of Adult Patients with NonAdvanced Systemic Mastocytosis Receiving Bezuclastinib 100 mg in the Ongoing Summit Trial: A Randomized, Double-Blind, Placebo Controlled Phase 2 Clinical Trial of Bezuclastinib

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Introduction: Bezuclastinib (CGT9486) is an investigational oral, selective tyrosine kinase inhibitor with demonstrated clinical activity and acceptable tolerability in advanced and non-advanced (NonAdv) systemic mastocytosis (SM).

Methods: Summit (NCT05186753) is a Phase 2, randomized, double-blind, placebo-controlled trial of bezuclastinib in patients with NonAdvSM and inadequate control of symptoms despite treatment with best supportive care (BSC). Part 1a randomized patients 1:1:1 to placebo, 100mg, or 200mg original formulation; Part 1b randomized 1:1:1 to placebo, 100mg, or 150mg optimized formulation. An open-label extension (OLE) follows Part 1 completion.

Results: Eighteen patients in Part 1 received 100 mg bezuclastinib original/optimized (bezu-100) and 19 received placebo. At baseline, patients received 2 (43%), 3 (24%), or ≥4 (32%) BSC medications. At week 12, the majority of TEAEs were low-grade and reversible without dose modifications; most common were hair color changes, nausea, and diarrhea. Robust reductions in disease biomarkers were observed with bezu-100: 94.4%, 100%, and 92.3% of patients had ≥50% reduction in serum tryptase, *KIT* p.D816V variant allele frequency, and bone marrow MCs, respectively. Mastocytosis Symptom Severity Daily Diary Total Symptom Score (MS2D2, a novel, disease-specific, patient-reported outcome measure) reduced from baseline by 49.1% with bezu-100 vs 21.1% with placebo. Seventeen patients continued bezu-100 in OLE and demonstrated further symptom improvement with reduction in MS2D2 by 59.7% at week 24 (datacut 14Mar2024). TEAEs observed in OLE were comparable to Part 1.

Conclusions: Favorable safety and clinically meaningful improvements in symptoms were demonstrated with bezu-100 at 12 weeks in Part 1 that continued into OLE.

Funding: **Cogent Biosciences**

S32

Updated Efficacy and Safety Results of Patients Receiving Selected 100 mg Bezuclastinib Dose and Participating in the Open-Label Extension of Summit: A Randomized, Double-Blind, Placebo Controlled Phase 2 Clinical Trial of Bezuclastinib in Adult Patients with NonAdvanced Systemic Mastocytosis

Lindsay A. M. Rein, Daniel J. DeAngelo, Brian D. Modena, Stephen T. Oh, Cristina Bulai Livideanu, Celalettin Ustun, Nathan Boggs, Michael Manning, Anthony M. Hunter, Cem Akin, Arnold Kirshenbaum, Ingunn Dybedal, Cecilia Arana Yi, Richard Herrscher, Mariana Castells, Frederick Lansigan, Tracy I. George, Jay Patel, Lei Sun, Nisha Shah, Jenna Zhang, Amanda Pilla, Priya Singh, Rachael Easton, Frank Siebenhaar, Prithviraj Bose

Background: Bezuclastinib (CGT9486) is an investigational oral, selective tyrosine kinase inhibitor with demonstrated clinical activity and acceptable tolerability in advanced and non-advanced (NonAdv) systemic mastocytosis (SM).

Methods: Summit (NCT05186753) is a Phase 2, randomized, double-blind, placebo-controlled trial of bezuclastinib in patients with NonAdvSM and inadequate control of symptoms despite treatment with best supportive care (BSC). Part 1a randomized patients 1:1:1 to placebo, 100mg, or 200mg original formulation; Part 1b randomized 1:1:1 to placebo, 100mg, or 150mg optimized formulation. An open-label extension (OLE) follows Part 1 completion.

Results: Eighteen patients in Part 1 received 100 mg bezuclastinib original/optimized (bezu-100) and 19 received placebo. At baseline, patients received 2 (43%), 3 (24%), or ≥4 (32%) BSC medications. At week 12, the majority of TEAEs were low-grade and reversible without dose modifications; most common were hair color changes, nausea, and diarrhea. Robust reductions in disease biomarkers were observed with bezu-100: 94.4%, 100%, and 92.3% of patients had ≥50% reduction in serum tryptase, *KIT* p.D816V variant allele frequency, and bone marrow MCs, respectively. Pts treated with 100 mg bezu had reduction in Mastocytosis Symptom Severity Daily Diary Total Symptom Score (MS2D2, a novel, disease-specific, patient-reported outcome measure) TSS by 49.1% vs 21.1% with PBO. On a 0-10 scale, the most severe MS2D2 symptom mean change from BL was -3.03 from a BL mean of 7.6 with bezu vs -1.04 from a BL mean of 7.7 with PBO. Individual symptoms of the MS2D2 TSS, as well as others not in the TSS including diarrhea and brain fog, improved more with bezu than with PBO

Conclusions: Favorable safety and clinically meaningful improvements in all individual MS2D2 TSS symptoms and across domains were demonstrated with bezu-100 at 12 weeks in Part 1 that continued into OLE.

Funding: **Cogent Biosciences**

S37

Correlation between Subjective and Objective Disease Control in Hereditary Angioedema: Association between the Angioedema Control Test and Attack Rate

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Introduction: Angioedema Control Test (AECT) is a validated, self-reported instrument capturing subjective control of angioedema attacks in patients with recurrent angioedema, including hereditary angioedema (HAE). Current analyses evaluated correspondence between subjective disease control (AECT scores) and objective disease control (HAE attack rate) in patients with HAE.

Methods: In the phase 3, double-blind, placebo-controlled OASIS-HAE study (NCT05139810), patients with HAE were randomized to donidalorsen 80 mg or placebo subcutaneously over 24 weeks. AECT was administered at Baseline (Week 0) and every 4 weeks through Week 24. AECT is scored as 0-16 points; higher scores indicate better disease control, with scores ≥10 indicating well-controlled disease. Time-normalized, investigator-confirmed HAE attack rate was captured from Week 0 through Week 24. Post hoc analyses, which included all dosed patients (N=90), used attack rates over the previous 4 weeks to match the AECT recall period.

Results: At Weeks 0 and 24, Spearman correlations of –0.40 and –0.78 were observed between AECT scores and attack rates, and -0.58 between changes in AECT scores and attack rates from Week 0 to Week 24. At Week 24, mean attack rates differed substantially between well-controlled and poorly-controlled subgroups (0.24 vs. 3.29, $p<0.001$, Cohen's $d=2.03$). At Week 24, 37 of 38 (97.4%) patients reporting complete control (AECT=16) had an attack rate of 0, while patients with an attack rate of 0 over the previous month had mean AECT=15.1 vs. 7.7 for patients with attack rate >0.

Conclusions: Results support strong correlation between subjective (AECT) and objective (attack rate) disease control in patients with HAE.

Funding: Ionis Pharmaceuticals

S38

Hereditary Angioedema Disease Control After Switching To Donidalorsen From Prior Long-Term Prophylaxis: Results From The OASISplus Open-Label Extension Study

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Introduction: Hereditary angioedema (HAE) is a rare disease characterized by recurrent, frequently severe tissue swelling. Here, we report disease control results from a predefined 16-week analysis of the OASISplus open-label extension (NCT05392114) in patients switching from prior prophylaxis to donidalorsen, an investigational ligand-conjugated antisense oligonucleotide targeting prekallikrein production.

Methods: After a 10-week baseline period, patients with HAE on stable doses (≥12 weeks) of lanadelumab, C1 inhibitor (C1INH), or berotralstat switched, without washout, to donidalorsen 80 mg every 4 weeks, per a protocol-specified algorithm. Prespecified exploratory endpoints included changes in Angioedema Control Test (AECT; scored 0–16 with higher scores indicating better disease control; <10 indicates poorly-controlled disease, ≥10 indicates well-controlled disease) and HAE attack rate.

Results: As of February 2024, 64 patients switched to donidalorsen: 31 from lanadelumab; 22 from C1INH; 11 from berotralstat. Fifty-eight completed 16 weeks. From baseline to Week 16, mean AECT scores improved from 12.0 to 13.9 in patients switching from lanadelumab, 11.7 to 14.2 in patients switching from C1INH, and 8.7 to 13.4 in patients switching from berotralstat. The proportion of patients reporting well-controlled disease increased from 74% to 93% (lanadelumab), 65% to 95% (C1INH), and 50% to 90% (berotralstat). Overall, mean monthly HAE attack rates decreased by 65% (lanadelumab), 41% (C1INH), and 73% (berotralstat) from baseline to Week 16. In patients reporting poorly-controlled disease at baseline, mean monthly HAE attack rates decreased by 73% (lanadelumab), 60% (C1INH), and 76% (berotralstat).

Conclusions: Switching from lanadelumab, C1INH, or berotralstat to donidalorsen improved patient-reported disease control and reduced HAE attack rates.

Funding: Ionis Pharmaceuticals, Inc

S39

Epinephrine Delivered via Sublingual Film (Anaphylm™) Elicits Rapid and Consistent Pharmacokinetic and Pharmacodynamic Responses

Carl Kraus, MD, Nils Confer, PhD, David Golden, MD, David Bernstein, MD, Matthew Greenhawt, MD

Introduction: Epinephrine is the first-line treatment for severe allergic reactions, including anaphylaxis. Prompt, reliable treatment is critical for patient outcomes. Anaphylm is a sublingual film containing a novel prodrug of epinephrine in development for the treatment of Type I allergic reactions, including anaphylaxis.

Methods: A phase 3 cross-over trial (AQ109301) was conducted in 64 healthy adults evaluating the pharmacokinetics (PK, including time to peak plasma concentration [T_{max}]) and pharmacodynamics (PD, heart rate [HR], systolic [SBP] and diastolic blood pressure [DBP]) of Anaphylm compared to epinephrine autoinjectors (EAI) and manual intramuscular epinephrine injection (IM).

Results: After single dose administration, the T_{max} variability as reflected by interquartile range (IQR) was 5.0 minutes (min) for Anaphylm (median T_{max} 12 min), 23.5 min for EpiPen (median T_{max} 20 min), 32.0 min for Auvi-Q (median T_{max} 30 min), and 15.0 min for manual IM injection (median T_{max} 50 min). After Anaphylm administration, clinically meaningful changes in median SBP, DBP, and HR were seen in 5 minutes (>10mmHg), 5 minutes (>10mmHg), and 8 minutes (>10bpm), respectively.

Conclusion: Anaphylm data demonstrates a more rapid and consistent PK profile in comparison to EAIs and IM. Moreover, Anaphylm's PD profile showed clinically relevant increases in SBP, DBP, and HR. These results further support the development of sublingual epinephrine film as a reliable needle-free alternative for the treatment of Type I allergic reactions, including anaphylaxis.

Funding: Aquestive Therapeutics, Inc.

S40

The Physicochemical Properties of Anaphylm™ Under Extreme Temperatures and Real-World Conditions

Nils Confer, PhD, Vincent Buono[1], Gregory Tsodikov, Carl Kraus, MD

Rationale: During an emergency allergic reaction, access to and prompt administration of epinephrine correlates with improved patient outcomes. In support, the drug product and packaging must withstand extreme temperatures and real-world conditions resulting from varied lifestyles in which the emergency use medication needs to be available. Anaphylm is a sublingual film that contains a novel prodrug of epinephrine packaged with the intent to support each potential patient use situation.

Methods: Packaging and drug product were subjected to temperatures outside of acceptable storage conditions (excursions) followed by long-term storage. Additional testing involved exposure to water submersion and fold endurance. Package integrity and retained drug product potency were evaluated, as were dissolution profiles when either at elevated or freezing temperatures.

Results: Potency prior to temperature exposures was 102.2% LC. After exposure to 50°C for 28 days, potency was 97.7% LC and 96.9% LC after 12 months at 25°C/60% RH post-excursion. After exposure to 60°C for 21 days, potency was 97.3% LC and 95.2% LC after 12 months at 25°C/60% RH post-excursion. After exposure to 70°C for 7 days, the potency was 96.6% LC and 91.7% LC after 12 months at 25°C/60% RH post-excursion. When frozen and thawed to 25°C, 40°C, and 60°C, the potency after 12 months at 25°C/60% RH post-excursion was 98.0%, 100.7%, and 99.0%, respectively. When submerged in 25°C water for 7 days or 60°C water for 30 or 60 minutes, no significant change in water content was observed. Fold tests did not reduce packaging integrity or film usability. Dissolution tests immediately after freezing to -80ºC or heating to 70ºC demonstrated consistent drug release.

Conclusion: Anaphylm demonstrated desirable physicochemical properties regarding both packaging and film stability. Performance attributes suggest that Anaphylm has the potential to be a unique epinephrine rescue medication with stability and usability properties not possible with liquid-based epinephrine products.

Funding: Aquestive Therapeutics, Inc.

S41

Investigator- and patient-rated local tolerability in phase 3 trials of topical roflumilast in patients with psoriasis, seborrheic dermatitis, and atopic dermatitis

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Introduction: Many topical prescription products use penetration enhancers to help overcome barrier properties of the skin; however, these may cause tolerability reactions (eg, burning/stinging), potentially reducing treatment adherence. Topical roflumilast is a highly potent phosphodiesterase 4 inhibitor formulated as a water-based cream or foam that does not contain penetration enhancers or fragrances. Investigator- and patient-rated application-site tolerability from phase 3 trials of topical roflumilast for patients with psoriasis (DERMIS-1, DERMIS-2, ARRECTOR), seborrheic dermatitis (SD; STRATUM), and atopic dermatitis (AD; INTEGUMENT-1, INTEGUMENT-2) were prospectively assessed.

Methods: Randomized patients applied topical roflumilast (DERMIS-1/2: 0.3% cream; ARRECTOR and STRATUM: 0.3% foam; INTEGUMENT-1/2: 0.15% cream) or vehicle foam or cream once daily for 8 weeks (DERMIS-1/2, ARRECTOR, and STRATUM) or 4 weeks (INTEGUMENT-1/2). Investigators assessed application-site tolerability on an 8-point scale (0 [no evidence of irritation] to 7 [strong reaction spreading beyond application site]) in the clinic before application of study treatment. Patient-reported application-site tolerability was rated on a 4-point scale (0 [no sensation] to 3 [hot, tingling/stinging sensation that has caused definite discomfort]) in the clinic 10–15 minutes after application. Tolerability was also assessed by reviewing adverse events.

Results: Investigators reported ≥96.5% of patients in the roflumilast-treated groups had no evidence of application-site irritation across all trials and timepoints. Patient-rated tolerability improved with treatment; across all trials, 1% of patients treated with roflumilast reported a hot, tingling/stinging sensation that has caused definite discomfort after the first application (day 1) and <1% at each subsequent assessment. Rates of adverse events, including those at the application site, were low for all trials.

Conclusions: Roflumilast cream and foam formulations demonstrated favorable application-site tolerability profiles based on investigator- and patient-rated assessments in patients with psoriasis, SD, or AD, including application to thin-skinned areas, such as the face and intertriginous areas.

Funding: Arcutis Biotherapeutics, Inc.

S42

Patient-reported outcomes and family impact with roflumilast cream 0.15% in atopic dermatitis: pooled results from phase 3 INTEGUMENT-1 and INTEGUMENT-2 trials

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Introduction: Roflumilast cream 0.15%, a potent phosphodiesterase 4 inhibitor, is approved for once-daily treatment of atopic dermatitis (AD) in patients aged ≥6 years. Pooled data from identically designed phase 3 randomized controlled trials (INTEGUMENT-1/NCT04773587; INTEGUMENT-2/NCT04773600) were used to evaluate the impact of roflumilast cream 0.15% on patient-reported outcomes (including family impact).

Methods: Patients aged ≥6 years with AD, Eczema Area and Severity Index ≥5, and Validated Investigator Global Assessment for AD (vIGA-AD) of mild or moderate were randomized 2:1 to apply once-daily roflumilast cream 0.15% or vehicle cream for 4 weeks. The primary endpoint was vIGA-AD success (clear/almost clear plus ≥2-grade improvement from baseline) at week 4. Changes from baseline in SCORing AD (SCORAD) total score (minimally important difference [MID]: −8.7), Patient-Oriented Eczema Measure (POEM; MID: −3.4), Dermatitis Family Impact (DFI) in patients aged ≤17 years (MID: not established), safety, and tolerability were assessed.

Results: A significantly greater proportion of the roflumilast (n=884) versus vehicle (n=453) group (31.3% vs 14.1%; $P<0.0001$) achieved vIGA-AD success at week 4. Patients treated with roflumilast versus vehicle also had greater mean percent improvement in SCORAD total score (46.2% vs 26.6%; $P<0.0001$) and least-squares mean improvements in POEM (7.5 vs 3.9; $P<0.0001$) and DFI (3.12 vs 1.74; $P<0.0001$) at week 4. Higher proportions of patients in the roflumilast versus vehicle groups achieved MID for SCORAD (78.9% vs 54.9%, respectively; $P<0.00001$) and POEM (72.9% vs 49.5%; $P<0.00001$). Roflumilast and vehicle were associated with low incidences of treatment-related adverse events (6.0% and 2.7%, respectively) and treatment-emergent adverse events leading to discontinuation of the trial or trial drug (1.6% and 1.1%, respectively).

Conclusions: In phase 3 trials of patients with AD aged ≥6 years, once-daily roflumilast cream 0.15% improved signs and symptoms of AD, patient-reported outcomes, and family impact.

Funding: Arcutis Biotherapeutics, Inc

S43

Efficacy and safety of once-daily roflumilast cream 0.05% in pediatric patients aged 2– 5 years with mild-to-moderate atopic dermatitis: a phase 3 randomized controlled trial (INTEGUMENT-PED)

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Introduction: Roflumilast cream 0.15% is a highly potent phosphodiesterase 4 inhibitor approved for once-daily use in patients aged ≥6 years with mild-to-moderate atopic dermatitis (AD). The INTEGUMENT-PED/NCT04845620 trial was conducted to evaluate the efficacy and safety of once-daily roflumilast cream 0.05% in pediatric patients aged 2–5 years with mild-to-moderate AD.

Methods: In this phase 3 randomized, parallel-group, double-blind, vehicle-controlled trial, parents/caregivers of children aged 2–5 years with mild-to-moderate AD applied roflumilast cream 0.05% or vehicle cream once daily for 4 weeks. The primary efficacy endpoint was the proportion of patients who achieved Validated Investigator Global Assessment for AD (vIGA-AD) success (clear/almost clear with ≥2-grade improvement from baseline) at week 4. Secondary endpoints included proportion of patients who achieved ≥75% improvement in Eczema Area and Severity Index (EASI-75) and Worst Itch-Numeric Rating Scale (WI-NRS) success (≥4-point improvement in patients with baseline WI-NRS score ≥4); safety and tolerability were also assessed.

Results: Overall, 437 patients received roflumilast and 215 received vehicle. At week 4, significantly greater proportions of patients treated with roflumilast versus vehicle achieved vIGA-AD success (25.4% vs 10.7%; $P<0.0001$), EASI-75 (39.4% vs 20.6%; $P<0.0001$), and WI-NRS success (35.3% vs 18.0%; nominal $P=0.0002$). Improvement in itch was observed by 24 hours after first application (nominal $P=0.0014$). Incidence of treatment-related adverse events (AEs) was low in both treatment groups, with most being mild or moderate. Treatment-emergent AEs reported for >2% of patients and greater in the roflumilast group were upper respiratory tract infection, diarrhea, and vomiting. For application-site tolerability, >92% of patients treated with roflumilast reported no or mild sensation at any timepoint.

Conclusions: In this phase 3 trial, once-daily roflumilast cream 0.05% was well tolerated and improved AD in pediatric patients aged 2–5 years.

Funding: **Arcutis Biotherapeutics, Inc.**

S44

HAE Attack Rates in Pediatric Patients 2 to <12 Years of Age with Prophylactic Berotralstat: Results from Interim Analysis of APeX-P

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Introduction: Hereditary angioedema (HAE) is a rare, life-threatening disease characterized by recurrent painful swelling of the face, extremities, abdomen, and airways. HAE symptoms often occur early in life; current approved prophylactic treatments for children aged <12 years are limited and require parenteral administration. Berotralstat is an oral, small-molecule plasma kallikrein inhibitor for prophylaxis of HAE attacks.

Methods: APeX-P is an ongoing, open-label study evaluating the pharmacokinetics (PK), safety, and effectiveness of berotralstat in participants aged 2 to <12 years with HAE. Before berotralstat initiation, participants received standard of care for 12 weeks that could include long-term prophylaxis. PK characterization, HAE attack rates up to Month 12 (Week 48), and incidence of adverse events (AEs) were assessed in this interim analysis.

Results: Participants (N=29) had a median (range) age of 8.0 (3–11) years, and 48.3% were female. Median (range) age at HAE symptom onset was 2.0 (0.3–8.0) years; most (82.8%) had onset before the age of 6 years. As of interim data analysis, median (range) berotralstat dosing duration was 48.1 (12.1–73.0) weeks. Median (range) monthly attack rate in the standard-of-care period was 0.96 (0–5.0). Median (range) HAE monthly attack rates from Months 1 to 12 were 0 (Month 1: 0–4.0; Month 12: 0–1.7). The most commonly reported treatment-emergent AEs (TEAEs) were nasopharyngitis (27.6%), upper respiratory tract infection (24.1%), and headache (13.8%). There were no drug-related Grade 3/4 TEAEs, serious drug-related TEAEs, deaths, or discontinuations related to TEAEs.

Conclusions: The ongoing APeX-P study is the largest trial of long-term prophylaxis in patients with HAE aged 2 to <12 years, to date. Berotralstat was well tolerated and resulted in early and sustained reduction in monthly attack rates.

Funding: **BioCryst Pharmaceuticals, Inc.**

S45

The Use of neffy (Epinephrine Nasal Spray) to Treat Anaphylaxis During an Oral Food Challenge

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Introduction: Oral food challenges (OFCs) are performed under medical supervision to confirm or rule out food allergies. During a challenge, mild to severe allergic reactions can occur. This case report highlights the use of neffy (epinephrine nasal spray), approved by the U.S. FDA in August 2024, as an alternative to injectable epinephrine for treating allergic reactions, including anaphylaxis.

Methods: A 12-year-old male with a history of peanut allergy underwent a pre-planned OFC to evaluate the persistence of peanut allergy diagnosis. The patient's history included mild peanut reactions as a younger child. Serum-specific IgE testing, component testing, and skin prick testing remained mildly elevated; however, a recent accidental ingestion of peanut flour in a granola bar had not induced allergic symptoms. The patient and family wished to know if he continued to carry a peanut allergy diagnosis. During the challenge, incremental doses of peanut protein were administered under close observation.

Results: Approximately 2.5 hours after consuming a cumulative dose of around 5 grams of peanut protein, the patient developed delayed anaphylaxis characterized by sneezing, nasal congestion, flushing, urticaria, wheezing, and gastrointestinal cramping. Patient intranasal administration of neffy 2mg resulted in rapid, significant symptom improvement with no adverse effects other than mild localized vasoconstriction near the application site. The patient fully recovered with no recurrence of symptoms and retained a peanut allergy diagnosis.

Conclusions: This case demonstrated that neffy offers a safe and effective alternative to injectable epinephrine, providing a painless and easy-to-use method for delivering epinephrine. Its approval expands treatment options for anaphylaxis, particularly for individuals who are needle-adverse or untrained, thereby promoting timely and effective management of allergic reactions in both clinical and non-clinical settings.

Funding: ARS Pharmaceuticals, Inc.

S46

Successful usage of intranasal epinephrine during in-office anaphylaxis, a case series of three pediatric patients in real-world setting

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Introduction: Anaphylaxis is a severe, potentially fatal allergic reaction requiring immediate treatment. The primary intervention is epinephrine administration, often via auto-injectors. However, underutilization of auto-injectors is a persistent issue, influenced by factors such as needle anxiety and delayed symptom recognition, leading to worsened patient outcomes. Early administration of epinephrine significantly mitigates the risk of respiratory failure, cardiovascular collapse, and mortality, emphasizing the critical nature of prompt intervention. Delays in epinephrine administration are linked to complications such as biphasic anaphylaxis, prolonged recovery, and increased healthcare costs.The recent FDA approval of intranasal epinephrine, branded as "*neffy*," offers an innovative solution to common barriers in anaphylaxis treatment. This needle-free delivery method addresses the psychological hesitancy associated with auto-injectors, particularly among children and caregivers. Its ease of use and portability encourage consistent carrying and immediate application during anaphylaxis onset.

Methods: We present a case series of our experience with 3 pediatric patients treated with *neffy* during in-office food challenges.

Results: Our experience demonstrates the efficacy of intranasal epinephrine, achieving clinical outcomes comparable to traditional injectable formats.

Conclusion: By simplifying the administration process and reducing needle-related anxiety, intranasal epinephrine enhances adherence to treatment protocols and facilitates timely intervention. These advancements promise to significantly improve management outcomes for individuals at risk of anaphylaxis, ensuring both safety and efficacy in life-threatening situations.

Funding: ARS Pharmaceuticals, Inc